Paul Schulwitz

Access DB# 164245

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rebecca Cook Examiner #: 69826 Date: 8/29/05

Art Unit: 1614 Phone Number 30 Serial Number:

Mail Box and Bldg/Room Location: 3C70 Results Format Preferred (circle): PAPER DISK E-MAIL

3A71

If more than one search is submitted, please prioritize searches in order of need. MEJ

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention:

Inventors (please provide full names): All attached

Earliest Priority Filing Date:

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please provide structure for dervygpride + search it in a method of use to potentiate analgesic or allow for reduced amount of analgesics.

Claims are attached

Thanks you
Rebecca

need by 9/15/05

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed:	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time	Other		Other (specify)	

PTO-1590 (8-01)

Examiner Search notes

STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 164245

TO:	From:
Rebecca Cook **Location: rem/3A71/3C70** **Art Unit: 1614** **Thursday, September 15, 2005** **Case Serial Number: 10/622492**	**Paul Schulwitz** **Location: Biotech-Chem Library** **REM-1A65** **Phone: 571-272-2527** **Paul.schulwitz@uspto.gov**

Search Notes

Examiner Cook,

Please review the attached search results.
If you have any questions or if you would like to refine the search query, please feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
REM-1A65
571-272-2527

```
=> d his ful

     (FILE 'HOME' ENTERED AT 08:53:58 ON 15 SEP 2005)

     FILE 'HCAPLUS' ENTERED AT 08:54:40 ON 15 SEP 2005
                E US2003-622492/APPS
L1            4 SEA ABB=ON  PLU=ON  US2003-622492/AP
                SEL RN

     FILE 'REGISTRY' ENTERED AT 08:54:57 ON 15 SEP 2005
L2           73 SEA ABB=ON  PLU=ON  (437-38-7/BI OR 466-99-9/BI OR 57-27-2/BI
                OR 76-42-6/BI OR 103420-77-5/BI OR 125-28-0/BI OR 125-29-1/BI
                OR 127-35-5/BI OR 132875-61-7/BI OR 143-52-2/BI OR 20290-10-2/B
                I OR 20594-83-6/BI OR 27203-92-5/BI OR 357-56-2/BI OR 359-83-1/
                BI OR 42408-82-2/BI OR 465-65-6/BI OR 467-83-4/BI OR 467-84-5/B
                I OR 469-62-5/BI OR 52-26-6/BI OR 52485-79-7/BI OR 54340-58-8/B
                I OR 561-27-3/BI OR 57-42-1/BI OR 64-31-3/BI OR 71195-58-9/BI
                OR 76-41-5/BI OR 76-57-3/BI OR 76-99-3/BI OR 77-07-6/BI OR
                77-20-3/BI OR 915-30-0/BI OR 103420-82-2/BI OR 25322-68-3/BI
                OR 468-10-0/BI OR 57-50-1/BI OR 77-92-9/BI OR 9004-34-6/BI OR
                9005-25-8/BI OR 103-90-2/BI OR 106392-12-5/BI OR 110-15-6/BI
                OR 1119-97-7/BI OR 12441-09-7/BI OR 124417-48-7/BI OR 14807-96-
                6/BI OR 151-21-3/BI OR 15307-86-5/BI OR 25322-69-4/BI OR
                25618-55-7/BI OR 337376-15-5/BI OR 50-21-5/BI OR 50-70-4/BI OR
                50-99-7/BI OR 5138-18-1/BI OR 541-15-1/BI OR 557-04-0/BI OR
                56-81-5/BI OR 57-55-6/BI OR 577-11-7/BI OR 63-42-3/BI OR
                67889-72-9/BI OR 69-65-8/BI OR 69-79-4/BI OR 7447-40-7/BI OR
                7647-14-5/BI OR 7757-93-9/BI OR 7778-18-9/BI OR 8044-71-1/BI
                OR 87-69-4/BI OR 9005-32-7/BI OR 9005-37-2/BI)

     FILE 'HCAPLUS' ENTERED AT 08:55:03 ON 15 SEP 2005
L3            4 SEA ABB=ON  PLU=ON  L1 AND L2
                D L3 IALL HITSTR 1-4

     FILE 'REGISTRY' ENTERED AT 08:59:37 ON 15 SEP 2005
                E DEVAZEPIDE/CN
L4            1 SEA ABB=ON  PLU=ON  DEVAZEPIDE/CN
                D
L5              STR 103420-77-5
L6            7 SEA SSS SAM L5
L7            0 SEA FAM SAM L5
L8            6 SEA FAM FUL L5
                SEL RN
L9            6 SEA ABB=ON  PLU=ON  (103343-54-0/CRN OR 103420-77-5/CRN OR
                103420-82-2/CRN OR 119702-76-0/CRN OR 119702-77-1/CRN OR
                119818-01-8/CRN) OR L8

     FILE 'HCAPLUS' ENTERED AT 09:01:08 ON 15 SEP 2005
L10         308 SEA ABB=ON  PLU=ON  L9
                E ANALGESICS/CT
                E E3+ALL
L11      102056 SEA ABB=ON  PLU=ON  ANALGESICS+PFT,NT,RTCS/CT
                E OPIOIDS/CT
                E E3+ALL
L12       31938 SEA ABB=ON  PLU=ON  OPIOIDS+PFT,NT/CT
                E ANALGESIA/CT
                E E3+ALL
L13       33365 SEA ABB=ON  PLU=ON  ANALGESIA+PFT,RTCS/CT
L14      106183 SEA ABB=ON  PLU=ON  L11 OR L12 OR L13
```

```
L15          38 SEA ABB=ON  PLU=ON  L10 AND L14
L16          30 SEA ABB=ON  PLU=ON  L10 AND ANALGES?
L17          40 SEA ABB=ON  PLU=ON  L15 OR L16
L18           4 SEA ABB=ON  PLU=ON  L17 AND L3

     FILE 'MEDLINE' ENTERED AT 09:04:02 ON 15 SEP 2005
L19         687 SEA ABB=ON  PLU=ON  L9
                E ANALGESICS/CT
                E E3+ALL
L20      354271 SEA ABB=ON  PLU=ON  ANALGESICS+PFT,NT/CT
                E OPIOIDS/CT
                E E3+ALL
                E E2+ALL
L21       80908 SEA ABB=ON  PLU=ON  NARCOTICS+PFT,NT/CT
                E ANALGESIA/CT
                E E3+ALL
L22       21591 SEA ABB=ON  PLU=ON  ANALGESIA+PFT,NT/CT
L23          61 SEA ABB=ON  PLU=ON  L19 AND (L20 OR L21 OR L22)
L24          60 SEA ABB=ON  PLU=ON  L23 NOT PY>2002
                D TRIAL 1-5

     FILE 'EMBASE' ENTERED AT 09:07:00 ON 15 SEP 2005
L25        1158 SEA ABB=ON  PLU=ON  L9
                E ANALGESICS/CT
                E E3+ALL
                E ANALGESICS/CT
                E E6+ALL
                E E2+ALL
L26      132755 SEA ABB=ON  PLU=ON  NARCOTIC ANALGESIC AGENT+PFT,NT/CT
L27          78 SEA ABB=ON  PLU=ON  L26 AND L25
L28          73 SEA ABB=ON  PLU=ON  L27 NOT PY>2002

     FILE 'HCAPLUS' ENTERED AT 09:09:00 ON 15 SEP 2005


     FILE HOME

     FILE HCAPLUS

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     FILE COVERS 1907 - 15 Sep 2005  VOL 143 ISS 12
     FILE LAST UPDATED: 14 Sep 2005  (20050914/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

      This file contains CAS Registry Numbers for easy and accurate
      substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
```

provided by InfoChem.

STRUCTURE FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2
DICTIONARY FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE MEDLINE
FILE LAST UPDATED: 14 SEP 2005 (20050914/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 9 Sep 2005 (20050909/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil hcap
FILE 'HCAPLUS' ENTERED AT 09:09:18 ON 15 SEP 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

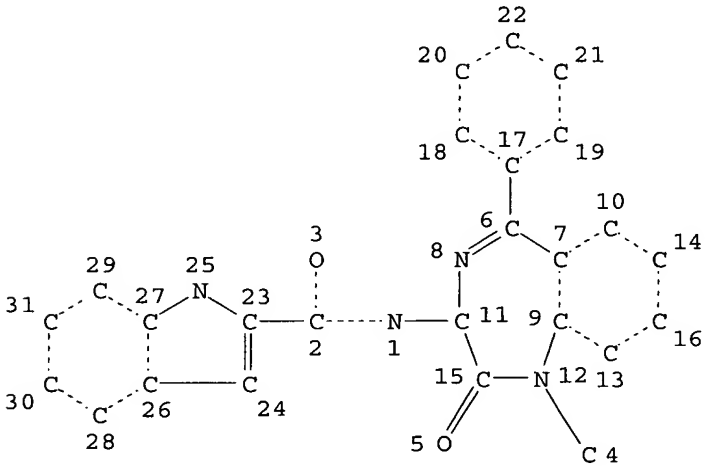
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 15 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 14 Sep 2005 (20050914/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat l17
L5 STR

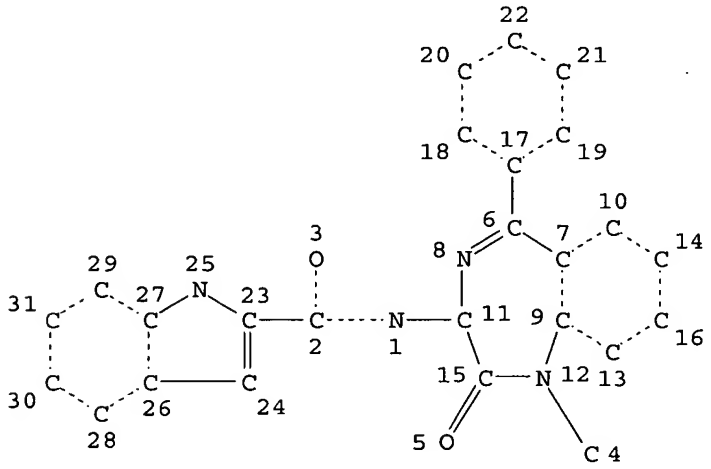


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE
L8 6 SEA FILE=REGISTRY FAM FUL L5
L9 6 SEA FILE=REGISTRY ABB=ON PLU=ON (103343-54-0/CRN OR 103420-77-5/CRN OR 103420-82-2/CRN OR 119702-76-0/CRN OR 119702-77-1/CRN OR 119818-01-8/CRN) OR L8
L10 308 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L11 102056 SEA FILE=HCAPLUS ABB=ON PLU=ON ANALGESICS+PFT,NT,RTCS/CT
L12 31938 SEA FILE=HCAPLUS ABB=ON PLU=ON OPIOIDS+PFT,NT/CT

```
L13         33365 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANALGESIA+PFT,RTCS/CT
L14        106183 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L12 OR L13
L15            38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L14
L16            30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND ANALGES?
L17            40 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 OR L16

=> fil medline
FILE 'MEDLINE' ENTERED AT 09:09:27 ON 15 SEP 2005

 FILE LAST UPDATED: 14 SEP 2005 (20050914/UP). FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available. For details enter HELP
 RLOAD at an arrow promt (=>). See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que stat l24
L5                  STR
```



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  31

STEREO ATTRIBUTES: NONE
L8              6 SEA FILE=REGISTRY FAM FUL L5
```

```
L9             6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (103343-54-0/CRN OR 103420-77
                 -5/CRN OR 103420-82-2/CRN OR 119702-76-0/CRN OR 119702-77-1/CRN
                  OR 119818-01-8/CRN) OR L8
L19          687 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9
L20       354271 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANALGESICS+PFT,NT/CT
L21        80908 SEA FILE=MEDLINE ABB=ON  PLU=ON  NARCOTICS+PFT,NT/CT
L22        21591 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANALGESIA+PFT,NT/CT
L23           61 SEA FILE=MEDLINE ABB=ON  PLU=ON  L19 AND (L20 OR L21 OR L22)
L24           60 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 NOT PY>2002


=> fil embase
FILE 'EMBASE' ENTERED AT 09:09:39 ON 15 SEP 2005
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 FILE COVERS 1974 TO 9 Sep 2005 (20050909/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d que stat l28
L5               STR
```

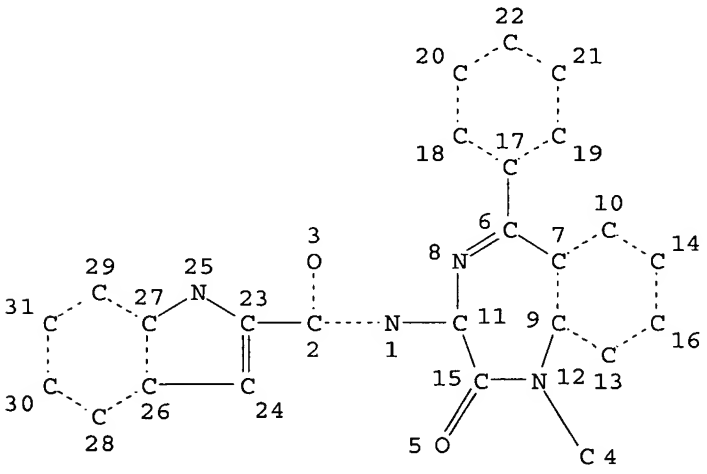

```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  31

STEREO ATTRIBUTES: NONE
L8             6 SEA FILE=REGISTRY FAM FUL L5
L9             6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (103343-54-0/CRN OR 103420-77
                 -5/CRN OR 103420-82-2/CRN OR 119702-76-0/CRN OR 119702-77-1/CRN
                  OR 119818-01-8/CRN) OR L8
L25         1158 SEA FILE=EMBASE ABB=ON  PLU=ON  L9
L26       132755 SEA FILE=EMBASE ABB=ON  PLU=ON  NARCOTIC ANALGESIC AGENT+PFT,NT
                 /CT
```

```
L27          78 SEA FILE=EMBASE ABB=ON  PLU=ON  L26 AND L25
L28          73 SEA FILE=EMBASE ABB=ON  PLU=ON  L27 NOT PY>2002


=> fil stng
FILE 'STNGUIDE' ENTERED AT 09:09:50 ON 15 SEP 2005
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep  9, 2005 (20050909/UP).

=> dup rem l24 l17 l28
FILE 'MEDLINE' ENTERED AT 09:10:15 ON 15 SEP 2005

FILE 'HCAPLUS' ENTERED AT 09:10:15 ON 15 SEP 2005
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PROCESSING COMPLETED FOR L24
PROCESSING COMPLETED FOR L17
PROCESSING COMPLETED FOR L28
L29          124 DUP REM L24 L17 L28 (49 DUPLICATES REMOVED)
                 ANSWERS '1-60' FROM FILE MEDLINE
                 ANSWERS '61-84' FROM FILE HCAPLUS
                 ANSWERS '85-124' FROM FILE EMBASE

=> d l29 ibib ab hitind 1-124

L29  ANSWER 1 OF 124     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2002636605     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12395894
TITLE:              Intestinal transit of fat depends on accelerating effect of
                    cholecystokinin and slowing effect of an opioid pathway.
AUTHOR:             Lin Henry C; Zaidel Oren; Hum Susan
CORPORATE SOURCE:   Department of Medicine, Cedars-Sinai Medical Center, CSMC
                    Burns & Allen Research Institute, Los Angeles, California
                    90048, USA.
SOURCE:             Digestive diseases and sciences, (2002 Oct) 47 (10)
                    2217-21.
                    Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        200211
ENTRY DATE:         Entered STN: 20021026
                    Last Updated on STN: 20021211
                    Entered Medline: 20021108
AB   Fat has been described to both accelerate and slow intestinal transit.  We
     hypothesized that the fat-induced jejunal brake depends on the combined
     accelerating effect of CCK and the slowing effect of an opioid pathway.
     Using a multifistulated model, intestinal transit was measured in four
     dogs, while 60 mM oleate was delivered into the proximal gut with either 0
     or 6 mg naloxone, and 0.1 mg/kg devazepide (a peripheral CCK-A-receptor
```

antagonist) administered intraluminally and intravenously, respectively. In a second study, intestinal transit was measured in seven dogs, while naloxone was delivered intraluminally at 0-, 3-, 6-, or 12-mg doses. Compared to the jejunal brake (marker recovery of 50.1 +/- 2.6%), intestinal transit was slowed by the CCK-A antagonist (36.4 +/- 8.3%; P < 0.05) and accelerated by naloxone (82.0 +/- 6.8%; P < 0.05). The accelerating effect of CCK occurred early in the transit response, while the dose-dependent effect (P < 0.05) of naloxone occurred later. We conclude that fat-induced jejunal brake depends on the early accelerating effect of CCK and the later slowing effect of a naloxone-sensitive opioid pathway.

CT Animals
Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: PH, physiology
Devazepide: PD, pharmacology
*Dietary Fats: ME, metabolism
Dogs
Dose-Response Relationship, Drug
Gastrointestinal Transit: DE, drug effects
*Gastrointestinal Transit: PH, physiology
Jejunum: DE, drug effects
Jejunum: PH, physiology
Naloxone: PD, pharmacology
Narcotic Antagonists: PD, pharmacology
Oleic Acid: ME, metabolism
Receptor, Cholecystokinin A
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: PH, physiology
*Receptors, Opioid: PH, physiology

RN **103420-77-5 (Devazepide)**; 112-80-1 (Oleic Acid); 465-65-6 (Naloxone); 9011-97-6 (Cholecystokinin)

CN 0 (Dietary Fats); 0 (Narcotic Antagonists); 0 (Receptor, Cholecystokinin A); 0 (Receptors, Cholecystokinin); 0 (Receptors, Opioid)

L29 ANSWER 2 OF 124 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000107198 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10640290
TITLE: Effects of spinal cholecystokinin receptor antagonists on morphine antinociception in a model of visceral pain in the rat.
AUTHOR: Friedrich A E; Gebhart G F
CORPORATE SOURCE: Department of Pharmacology, University of Iowa College of Medicine, Bowen Science Building, Iowa City, Iowa, USA.. ann-friedrich@uiowa.edu
CONTRACT NUMBER: F31 DA 05852 (NIDA)
NS 199121 (NINDS)
SOURCE: Journal of pharmacology and experimental therapeutics, (2000 Feb) 292 (2) 538-44.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309
Last Updated on STN: 20000309
Entered Medline: 20000222

AB The objective of the present study was to determine the effects of spinal cholecystokinin (CCK) receptor antagonists on morphine antinociception in

a model of visceral nociception, colorectal distension, in rats with chronic colonic inflammation and vehicle-treated controls. Three to five days after intracolonic instillation of 2,4,6-trinitrobenzenesulfonic acid (TNBS), an enhanced visceromotor response to all pressures of colorectal distension (10-80 mm Hg) was evident. The ED(50) of intrathecal morphine (0.93 microgram) in vehicle-treated rats produced significantly greater antinociception in TNBS-treated rats. Intrathecal proglumide, a nonselective CCK receptor antagonist, dose dependently enhanced the antinociceptive effect of morphine in vehicle-treated rats, but not in TNBS-treated rats. Similarly, L-365, 260, a specific CCK(B) receptor antagonist, dose dependently increased morphine's antinociceptive effects in vehicle-treated rats but had no effect in rats with TNBS-induced colonic inflammation. L-364,718, a specific CCK(A) receptor antagonist, had no effect on morphine antinociception in either vehicle-treated or TNBS-treated rats. These data indicate that CCK, acting at the CCK(B) receptor, is involved in modulating morphine antinociception following a noxious visceral stimulus. However, CCK receptor antagonists no longer enhance morphine antinociception after instillation of intracolonic TNBS, suggesting that visceral inflammation may lead to a reduction in spinal CCK release.

CT Check Tags: Male
***Analgesics: PD, pharmacology**
Anesthesia
Animals
Benzodiazepinones: PD, pharmacology
Colitis: PA, pathology
Colon: DE, drug effects
Devazepide: PD, pharmacology
Disease Models, Animal
Dose-Response Relationship, Drug
Drug Synergism
***Morphine: PD, pharmacology**
Phenylurea Compounds: PD, pharmacology
Proglumide: PD, pharmacology
Rats
Rats, Sprague-Dawley
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Rectum: DE, drug effects
Research Support, U.S. Gov't, P.H.S.
*Spinal Cord: DE, drug effects
Time Factors
Trinitrobenzenesulfonic Acid: TO, toxicity
*Viscera: DE, drug effects

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 2508-19-2 (Trinitrobenzenesulfonic Acid); 57-27-2 (Morphine); 6620-60-6 (Proglumide)

CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 3 OF 124 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2000441996 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10989941
TITLE: Role of cholecystokinin receptors in induction of antinociception in hot-plate test.
AUTHOR: Rezayat M; Rahnavard A; Zarrindast M R
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Iran.
SOURCE: Pharmacology & toxicology, (2000 Aug) 87 (2) 58-62. Journal code: 8702180. ISSN: 0901-9928.
PUB. COUNTRY: Denmark

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010109

AB In the present study, the antinociceptive effect of cholecystokinin receptor agonists in the hot-plate test in mice has been evaluated. Subcutaneous administration of cholecystokinin octapeptide (cholecystokinin-8; 0.001, 0.005, 0.01, 0.05, and 0.1 mg/kg), unsulfated cholecystokinin octapeptide (cholecystokinin-8U; 0.1 mg/kg) or caerulein (0.25 mg/kg) produced antinociception. Administration of the cholecystokinin tetrapeptide (cholecystokinin-4; 0.25, 0.5 and 1.0 mg/kg) had no effect in the hot-plate test. Subcutaneous injection of the selective cholecystokinin receptor antagonists, MK-329 (0.125, 0.25 and 0.5 mg/kg) or L-365,260 (0.125, 0.25 and 0.5 mg/kg), produced no antinociceptive response. When the animals were pretreated with the cholecystokinin receptor antagonists or naloxone (0.5 and 1 mg/kg), a significant decrease in the antinociceptive response induced by cholecystokinin-8 and caerulein was obtained. The results indicate that single administration of cholecystokinin receptor agonists could produce an antinociceptive effect which is probably mediated via cholecystokinin receptors. With respect to the results obtained from morphine and naloxone administration, it is concluded that there may be an interaction between cholecystokinin and opiate mechanisms.

CT Check Tags: Male
***Analgesia**
Analysis of Variance
Animals
Benzodiazepinones: PD, pharmacology
*Caerulein
Devazepide: PD, pharmacology
Dose-Response Relationship, Drug
Mice
Phenylurea Compounds: PD, pharmacology
*Receptors, Cholecystokinin: AG, agonists
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Sincalide

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 17650-98-5 (Caerulein); 25126-32-3 (Sincalide)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 4 OF 124 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000142578 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10678088
TITLE: Devazepide reversed effect of sincalide against morphine on rat jejunal activities.
AUTHOR: Xu M Y; Yang X P; Jin H B; Yang C X; Yang L Z
CORPORATE SOURCE: Department of Physiology, Harbin Medical University, China.
SOURCE: Zhongguo yao li xue bao = Acta pharmacologica Sinica, (1999 May) 20 (5) 419-22.
Journal code: 8100330. ISSN: 0253-9756.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005

ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000518

AB AIM: To study the antagonism of sincalide to the effect of morphine and its mechanism. METHODS: The electrophysiologic and mechanic activities of rat jejunum in vitro were recorded. RESULTS: Acetylcholine (ACh, 150 nmol.L-1) increased the spike potential amplitude (SPA) and the number (SPN) of rat jejunum in vitro, followed by an increase of jejunal contraction amplitudes (CA), showing a positive correlation. Morphine 330 nmol.L-1 inhibited the potentiation of ACh, showing a negative correlation. Sincalide 0.7 nmol.L-1 antagonized the effects of morphine, i.e., the SPA and SPN were increased again, followed by an increase of CA. CCK-A receptor antagonist devazepide (10 nmol.L-1) reversed the antagonism of sincalide to the effect of morphine. CONCLUSION: Sincalide antagonized the effect of morphine which inhibited the potentiation of ACh on jejunal activities in vitro. The antagonistic effect of sincalide on morphine was mainly mediated by CCK-A receptor.

CT Check Tags: Female; In Vitro; Male
Action Potentials: DE, drug effects
Animals
*Devazepide: PD, pharmacology
Dopamine Agents: PD, pharmacology
*Jejunum: PH, physiology
***Morphine: AI, antagonists & inhibitors**
*Muscle Contraction: DE, drug effects
Muscle, Smooth: PH, physiology
Rats
Rats, Wistar
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 57-27-2 (Morphine)

CN 0 (Dopamine Agents); 0 (Receptors, Cholecystokinin)

L29 ANSWER 5 OF 124 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999299815 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10372600
TITLE: The evaluation of the role of CCK in the opioid modulation of the motility of the gastrointestinal tract in sheep.
AUTHOR: Kania B F; Brikas P; Bueno L; Fioramonti J; Zaremba-Rutkowska M
CORPORATE SOURCE: Department of Veterinary Pharmacology and Toxicology, Veterinary Faculty, Warsaw Agricultural University SGGW, Poland.. wet_kfit@sggw.waw.pl
SOURCE: Journal of veterinary pharmacology and therapeutics, (1999 Apr) 22 (2) 153-60.
Journal code: 7910920. ISSN: 0140-7783.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 20000303
Entered Medline: 19991019

AB The participation of central cholecystokinin-8 (CCK-8) receptors in the modulatory effect of D-Ala2, N-Me-Phe4, Gly5-ol enkephalin (DAGO), a selective mu-opioid receptor agonist, on the spike burst activity of the

gastrointestinal tract (rumen, reticulum, antrum, duodenum, colon and caecum) in sheep was investigated. DAGO was infused intracerebroventricularly (i.c.v.) at doses of 0.1-1 microg/kg body weight (BW). It was shown that DAGO significantly inhibited myoelectrical activity of the wall of the forestomachs, abomasum and colon but stimulated this activity in the duodenum (rate of myoelectrical migrant complex-MMC). The effects of DAGO were prevented by CCK-8 antagonists (L-364.718 and L-365.260) previously infused at doses of 5-20 microg/kg BW. The results of this present study indicate that central receptors of CCK-8 participated in the modulatory action of an opioid on myoelectrical activity of the gastrointestinal tract in sheep. Furthermore, this result suggests that CCK-8 is released in response to mu-receptor stimulation, because CCK-8 antagonists (L-364.718 and L-365.260) prevented the modulatory action of DAGO on the gastrointestinal motility in sheep.

CT Check Tags: Female
Animals
Benzodiazepinones: PD, pharmacology
*Cholecystokinin: PH, physiology
Devazepide: PD, pharmacology
Electromyography
Enkephalin, Ala(2)-MePhe(4)-Gly(5)-
Enkephalins: AD, administration & dosage
Enkephalins: PD, pharmacology
*Gastrointestinal Motility: DE, drug effects
Injections, Intraventricular
Intestines: DE, drug effects
***Narcotics: PD, pharmacology**
Phenylurea Compounds: PD, pharmacology
Receptors, Cholecystokinin: DE, drug effects
Receptors, Cholecystokinin: PH, physiology
Receptors, Opioid, mu: AG, agonists
Receptors, Opioid, mu: PH, physiology
Research Support, Non-U.S. Gov't
Sheep
Stomach: DE, drug effects

RN 100929-53-1 (Enkephalin, Ala(2)-MePhe(4)-Gly(5)-); **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Enkephalins); 0 (Narcotics); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin); 0 (Receptors, Opioid, mu)

L29 ANSWER 6 OF 124 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999139770 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9974190
TITLE: Cholecystokinin receptor mechanism(s) and morphine tolerance in mice.
AUTHOR: Zarrindast M R; Nikfar S; Rezayat M
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Iran.
SOURCE: Pharmacology & toxicology, (1999 Jan) 84 (1) 46-50. Journal code: 8702180. ISSN: 0901-9928.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990517
Last Updated on STN: 19990517
Entered Medline: 19990506

AB In a previous work, the effects of cholecystokinin receptor agonists on

tolerance to morphine antinociception were evaluated. In the present study, the influence of cholecystokinin antagonists on the inhibition of tolerance to morphine antinociception by cholecystokinin agonists has been investigated. Maximum tolerance to morphine antinociception was obtained by morphine administration (50 mg/kg) to mice once daily for 4 days. The cholecystokinin receptor agonists caerulein (0.005 mg/kg) or cholecystokinin-8 (0.01 mg/kg) but not unsulfated cholecystokinin-8 (0.01 mg/kg) decreased the development of tolerance to morphine (9 mg/kg). The cholecystokininA receptor antagonist MK-329 (1 mg/kg) or the cholecystokininB receptor antagonist L-365,260 (0.25, 0.5 and 1 mg/kg) also diminished the tolerance to morphine antinociception. When animals were challenged with different doses of MK-329 (0.25, 0.5 and 1 mg/kg) against cholecystokinin-8 (0.01 mg/kg), caerulein (0.005 mg/kg) or unsulfated cholecystokinin-8 (0.01 mg/kg) on day 4 in tolerant mice, different response were obtained. Higher doses of MK-329 (1 mg/kg) caused a small decrease in attenuation of the morphine tolerance induced by cholecystokinin-8 and caerulein. Low doses of L-365, 260 diminished the effect of cholecystokinin-8 on morphine tolerance. Conversely high doses of the drug potentiated the response of caerulein (0.005 mg/kg). When animals were treated with MK-329 or L-365,260 before unsulfated cholecystokinin-8, reduction of the tolerance to morphine antinociception was obtained. These data indicate that both cholecystokinin receptors may modulate morphine tolerance.

CT Check Tags: Male
Animals
*Benzodiazepinones: PD, pharmacology
Caerulein: PD, pharmacology
Cholecystokinin: PD, pharmacology
*Devazepide: PD, pharmacology
Dose-Response Relationship, Drug
Drug Interactions
*Drug Tolerance: PH, physiology
Mice
***Morphine: PD, pharmacology**
Pain Measurement
*Phenylurea Compounds: PD, pharmacology
Random Allocation
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: PH, physiology
Time Factors

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 17650-98-5 (Caerulein); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 7 OF 124 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 1999180263 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10082226
TITLE: Cholecystokinin receptor agonists block the jumping behaviour precipitated in morphine-dependent mice by naloxone.
AUTHOR: Bourin M; Malinge M; Colombel M C; Vasar E
CORPORATE SOURCE: GIS Medicament, Department of Pharmacology, Faculty of Medicine, Nantes, France.
SOURCE: European neuropsychopharmacology : journal of the European College of Neuropsychopharmacology, (1999 Jan) 9 (1-2) 37-43.
Journal code: 9111390. ISSN: 0924-977X.
PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990526

AB The aim of present study was to reveal the role of cholecystokinin (CCK) in the jumping behaviour induced by the opioid antagonist naloxone (30 mg/kg) after the acute administration of morphine (200 mg/kg) in mice. Treatment with caerulein (0.01-1 microg/kg), a nonselective agonist of CCK receptors, induced a large reduction of jumping frequency without parallel suppression of locomotor activity. The CCK(B) receptor agonist CCK tetrapeptide (CCK-4. 0.125-32 mg/kg) caused the same effect, but it happened at much higher doses (above 0.5 mg/kg). Devazepide (1 microg/kg), a preferential CCK(A) receptor antagonist, completely reversed the action of caerulein (0.1 gmg/kg) and CCK-4 (2 mg/kg). A preferential CCK(B) receptor antagonists LY 288,513 at a high dose (4 mg/kg) blocked the action of CCK-4, but not that of caerulein. Acetorphan (16-128 mg/kg), an inhibitor of enkephalin metabolism, did not block naloxone-precipitated jumping behaviour. However, the combination of subthreshold doses of caerulein (0.001 microg/kg) and CCK-4 (0.25 mg/kg) with acetorphan (64 mg/kg) potently antagonized the behaviour induced by naloxone. In conclusion, the antagonism of CCK agonists against naloxone-precipitated jumping behaviour is apparently mediated via the CCK(A) receptor subtype. The stimulation of CCK(A) receptors seems to increase the release of endogenous enkephalins.

CT Check Tags: Male
Animals
Caerulein: PD, pharmacology
Devazepide: PD, pharmacology
Dose-Response Relationship, Drug
Hormone Antagonists: PD, pharmacology
Mice
*Morphine Dependence: PX, psychology
*Motor Activity: DE, drug effects
***Naloxone: PD, pharmacology**
*Narcotic Antagonists: PD, pharmacology
Pyrazoles: PD, pharmacology
*Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
*Substance Withdrawal Syndrome: DT, drug therapy
*Substance Withdrawal Syndrome: PX, psychology
Tetragastrin: AI, antagonists & inhibitors
Tetragastrin: PD, pharmacology
Thiorphan: AA, analogs & derivatives
Thiorphan: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 138932-35-1 (1-(4-bromophenylaminocarbonyl)-4,5-diphenyl-3-pyrazolidinone); 17650-98-5 (Caerulein); 1947-37-1 (Tetragastrin); 465-65-6 (Naloxone); 76721-89-6 (Thiorphan); 81110-73-8 (acetorphan)

CN 0 (Hormone Antagonists); 0 (Narcotic Antagonists); 0 (Pyrazoles); 0 (Receptors, Cholecystokinin)

L29 ANSWER 8 OF 124 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001248718 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11324560
TITLE: Antagonistic effect of CCK-8 on morphine-inhibited

electrical and contractile activities of rat jejunum in vitro.
AUTHOR: Xu M Y; Yang D X; Wang S Z; Jin H B; Zou X H; Yang X P; Han J S
CORPORATE SOURCE: Department of Physiology, Harbin Medical University, Harbin 150086.
SOURCE: Sheng li xue bao [Acta physiologica Sinica], (1998 Aug) 50 (4) 469-73.
Journal code: 20730130R. ISSN: 0371-0874.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB In the present investigation, antagonistic action of cholecystokinin octapeptide (CCK-8) against morphine on the electrical and contractile activity of rat jejunum in vitro was studied. The results showed that the potentiation of acetylcholine (ACh) on both the burst of spike and the contractility were inhibited by morphine, which could be completely antagonized by CCK-8. The CCK-8 effect, again, could be suppressed by CCK-A receptor antagonist devazepide (10 nmol/L), but partially by CCK-B receptor antagonist L-365, 260 at 10 nmol/L or completely at concentration of 30 nmol/L. The above results demonstrated that the antagonism of CCK-8 on morphine was mediated by both CCK-A and CCK-B receptors.

CT Check Tags: Comparative Study; Female; Male
Animals
Benzodiazepinones: PD, pharmacology
*Devazepide: PD, pharmacology
Electrophysiology
Jejunum: DE, drug effects
*Jejunum: PH, physiology
***Morphine: AI, antagonists & inhibitors**
*Muscle Contraction: DE, drug effects
Muscle, Smooth: DE, drug effects
*Muscle, Smooth: PH, physiology
Phenylurea Compounds: PD, pharmacology
Rats
Rats, Wistar
Receptor, Cholecystokinin A
Receptor, Cholecystokinin B
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 57-27-2 (Morphine)
CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin A); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 9 OF 124 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 97165453 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9013214
TITLE: Caerulein may potentiate morphine-induced antinociception by cholecystokinin-A and/or cholecystokinin-B receptor mechanisms.
AUTHOR: Rezayat M; Oreizi S; Zarrindast M R

CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Iran.
SOURCE: General pharmacology, (1997 Feb) 28 (2) 337-40.
Journal code: 7602417. ISSN: 0306-3623.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 19990129
Entered Medline: 19970819

AB 1. The effects of a cholecystokinin agonist and antagonist on morphine antinociception in the tail-flick test have been evaluated. 2. The administration of different doses of caerulein (0.01, 0.05 and 0.1 mg/kg) 30 min prior to morphine (1.5, 3 and 6 mg/kg) increased the antinociception induced by morphine in mice. 3. In animals pretreated with cholecystokinin antagonists MK-329 (0.125 and 0.25 mg/kg) and L-365,260 (0.125 and 0.25 mg/kg), the antinociceptive effect of morphine was not changed. However, high doses (0.5 mg/kg) of each antagonist potentiated the morphine response. 4. Low doses of cholecystokinin antagonists (0.125 and 0.25 mg/kg), that did not cause antinociception, when employed in combination with caerulein (0.05 mg/kg) decreased the response of morphine plus caerulein. 5. It is concluded that the cholecystokinin agonist caerulein potentiated the morphine response by stimulation of cholecystokinin-A and/or cholecystokinin-B receptors.

CT Check Tags: Male
***Analgesics, Opioid: PD, pharmacology**
Animals
Benzodiazepinones: PD, pharmacology
*Caerulein: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Drug Synergism
Mice
***Morphine: PD, pharmacology**
Pain Measurement: DE, drug effects
*Phenylurea Compounds
Receptor, Cholecystokinin A
Receptor, Cholecystokinin B
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: PH, physiology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 17650-98-5 (Caerulein); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Analgesics, Opioid); 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin A); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 10 OF 124 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 97256658 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9103499
TITLE: Antinociceptive effects of RB101, a complete inhibitor of enkephalin-catabolizing enzymes, are enhanced by a cholecystokinin type B receptor antagonist, as revealed by noxiously evoked spinal c-Fos expression in rats.
AUTHOR: Honore P; Buritova J; Fournie-Zaluski M C; Roques B P; Besson J M
CORPORATE SOURCE: Physiopharmacologie du Systeme Nerveux, l'Institut National de la Sante et de la Recherche Medicale U161, and Ecole

Pratique des HautesEtudes, Paris, France.
SOURCE: Journal of pharmacology and experimental therapeutics, (1997 Apr) 281 (1) 208-17.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19990129
Entered Medline: 19970502

AB The effects of RB101, a complete inhibitor of enkephalin-catabolizing enzymes, alone or with a selective cholecystokinin (CCK)B receptor antagonist (CI988) or CCK(A) receptor antagonist (devazepide), on carrageenin-induced spinal c-Fos expression were investigated. Spinal c-Fos expression was observed 90 min after intraplantar carrageenin (6 mg/150 microl saline), with Fos-like-immunoreactive neurons preferentially located in the superficial laminae of the spinal dorsal horn. Intravenous RB101 (10, 20 and 40 mg/kg) dose-dependently reduced the number of superficial Fos-like-immunoreactive neurons (r2 = 0.739, P < .0001), with 63 +/- 2% (P < .0001) reduction for the highest dose. These effects were completely blocked by coadministered naloxone. Coadministration of inactive doses of i.v. RB101 (5 mg/kg) and i.p. CI988 (3 mg/kg) significantly and strongly reduced the number of carrageenin-induced, superficial, Fos-like-immunoreactive neurons (55 +/- 5% reduction of control carrageenin c-Fos expression, P < .0001). This effect was blocked by coadministered naloxone. It is important to note that coadministered RB101 and devazepide did not influence spinal c-Fos expression. None of the various drug combinations influenced the carrageenin-induced peripheral edema. These results show that RB101 dose-dependently decreases carrageenin-evoked spinal c-Fos expression. In addition, the effectiveness of RB101 can be revealed by preadministration of the CCK(B) receptor antagonist CI988. Considering the weak opioid side effects obtained with RB101 treatment and the strong increase of its effects by the CCK(B) receptor antagonist, this type of drug combination could have promising therapeutic application in the management of pain in humans.

CT Check Tags: Male
***Analgesics: PD, pharmacology**
Animals
Benzodiazepinones: PD, pharmacology
Devazepide
*Disulfides: PD, pharmacology
Dose-Response Relationship, Drug
Edema: DT, drug therapy
*Enzyme Inhibitors: PD, pharmacology
*Indoles: PD, pharmacology
*Meglumine: AA, analogs & derivatives
Meglumine: PD, pharmacology
Pain: DT, drug therapy
*Pain: ME, metabolism
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Proto-Oncogene Proteins c-fos: AN, analysis
Rats
Rats, Sprague-Dawley
Receptor, Cholecystokinin B
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't

Spinal Cord: CH, chemistry
*Spinal Cord: DE, drug effects
RN **103420-77-5 (Devazepide)**; 130404-91-0 (PD 134308); 135949-60-9 (RB 101); 6284-40-8 (Meglumine); 63-91-2 (Phenylalanine)
CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Disulfides); 0 (Enzyme Inhibitors); 0 (Indoles); 0 (Proto-Oncogene Proteins c-fos); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 11 OF 124 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 97409741 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9264087
TITLE: Effects of caerulein and CCK antagonists on tolerance induced to morphine antinociception in mice.
AUTHOR: Zarrindast M R; Zabihi A; Rezayat M; Rakhshandeh H; Ghazi-Khansari M; Hosseini R
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Iran.
SOURCE: Pharmacology, biochemistry, and behavior, (1997 Sep) 58 (1) 173-8.
Journal code: 0367050. ISSN: 0091-3057.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971013
Last Updated on STN: 19990129
Entered Medline: 19970930

AB Different groups of mice received one daily dose (50 mg/kg) of morphine subcutaneously (SC) for 3, 4 or 5 days to develop tolerance to the opioid. The antinociceptive response of morphine (9 mg/kg) was tested in the hot-plate test 24 h after the last dose of the drug. Tolerance to morphine was obtained in all groups. The group of mice that received morphine for 4 days was employed for the rest of the experiments. Pretreatment of animals with a single dose of caerulein (0.025, 0.05, and 0.1 mg/kg, SC) 30 min prior to receiving morphine (50 mg/kg; during the development of tolerance to the opioid) on day 1, 2, 3, 4 or 5 of morphine administration potentiate antinociception induced by morphine (test dose of 9 mg/kg). The dose of 0.05 mg/kg of caerulein, used 30 min before morphine administration on day 3, was also used to evaluate the effects of antagonists on caerulein-induced decrease in tolerance. The selective cholecystokinin (CCK) receptor antagonists, MK-329 [1-methyl-3-(2 indoloyl)amino-5-phenyl-3H-1,4-benzodiazepin-2-one; 0.25 and 0.5 mg/kg] or L-365,260 [3R(+)-N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N-(3-methyl-phenyl)urea: 0.25 and 0.5 mg/kg] decreased potentiation of morphine response induced by caerulein. MK-329 or L-365,260, when were injected 35 min before morphine injection during the development of tolerance and on day 3, decreased the tolerance to morphine. A single administration of MK-329 or L-365,260 (in the absence of caerulein) 35 min and 48 h before the test dose of morphine (9 mg/kg) potentiated the antinociception of morphine in nontolerant animals. In conclusion, CCK mechanism(s) may interact with morphine tolerance.

CT Check Tags: Male
***Analgesics, Opioid: PD, pharmacology**
Animals
Benzodiazepinones: PD, pharmacology
*Caerulein: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide

Drug Tolerance
Mice
***Morphine: PD, pharmacology**
Pain Measurement: DE, drug effects
*Phenylurea Compounds
Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Time Factors
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 17650-98-5 (Caerulein); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Analgesics, Opioid); 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 12 OF 124 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 97169102 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9016909
TITLE: Antidepressant-like effects of CCK(B) receptor antagonists: involvement of the opioid system.
AUTHOR: Hernando F; Fuentes J A; Fournie-Zaluski M C; Roques B P; Ruiz-Gayo M
CORPORATE SOURCE: Departamento de Farmacologia, Facultad de Farmacia, Universidad Complutense, Ciudad Universitaria, Madrid, Spain.
SOURCE: European journal of pharmacology, (1996 Dec 30) 318 (2-3) 221-9.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19990129
Entered Medline: 19970529

AB RB 101 (N-[(R,S)-2-benzyl-3-[(S)-2-amino-4-methylthiobutyldithio]-1-oxopropyl]-L -phenylalaninebenzyl ester), a systemically active inhibitor of enkep halin catabolism, has been shown to elicit antidepressant-like effects in mice, both in the forced-swimming and in the conditioned suppression of the mobility tests. The same type of response has been also observed following administration of the cholecystokinin CCK(B) receptor antagonist L-365,260 ((3R)-(+)-N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin -3-yl)-3 -methylphenylurea). In terestingly, the delta-opioid receptor antagonist naltrindole (17-cyclopropylmethyl-6,7-dehydro-4,5alpha-epoxy-3,14-dihydroxy-6, 7,2'-3'-indolomorphinan) blocks the effect of both RB 101 and L-365,260 in the conditioned suppression of the motility test. In this work we have investigated the involvement of the opioid system in the antidepressant response to the CCK(B) receptor antagonist L-365,260 in the forced-swimming test in mice. The effect of L-365,260 was decreased by the delta-opioid receptor antagonist naltrindole. Furthermore, the CCK(B) receptor agonist, BC 264 (Boc-Tyr(OSO3H)-gNle-mGly-Trp-(NMe)Nle-Asp-Phe-NH2), blocked the antidepressant-like effect of RB 101 while CCK-8 (H-Asp-Tyr(OSO3H)-Met-Gly-Trp-Met-Asp-Phe-NH2) enhanced the effect of this drug, probably through stimulation of central CCK(A) receptors, since the CCK(A) receptor antagonist devazepide ((3S)-(-)-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin++ +-3-yl)-1H-indole-2 -carboxamide) abolished the CCK-8-induced potentiation of the RB 101 effect. In addition, RB 101 enhanced the effect of L-365,260. Such an effect was blocked by the delta-opioid receptor antagonist naltrindole. These data further support

the involvement of opioid receptors in the antidepressant-type effect induced by CCK(B) receptor blockers and support the hypothesis of a regulatory role of CCK in the activity of the endogenous opioid system. As in other experimental paradigms, CCK(A) and CCK(B) receptor stimulation appears to have opposite effects in modulating opioidergic activity.

CT Check Tags: Male
Animals
*Antidepressive Agents: PD, pharmacology
Benzodiazepinones: PD, pharmacology
Devazepide
Disulfides: PD, pharmacology
*Endorphins: PH, physiology
Mice
Naloxone: PD, pharmacology
Naltrexone: AA, analogs & derivatives
Naltrexone: PD, pharmacology
Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Phenylurea Compounds
Receptor, Cholecystokinin A
Receptor, Cholecystokinin B
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: PH, physiology
Research Support, Non-U.S. Gov't
Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 135949-60-9 (RB 101); 16590-41-3 (Naltrexone); 25126-32-3 (Sincalide); 465-65-6 (Naloxone); 63-91-2 (Phenylalanine); 72782-05-9 (beta-funaltrexamine)

CN 0 (Antidepressive Agents); 0 (Benzodiazepinones); 0 (Disulfides); 0 (Endorphins); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin A); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 13 OF 124 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 96432293 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8835359
TITLE: Effects of cholecystokinin receptor agonist and antagonists on morphine dependence in mice.
AUTHOR: Zarrindast M R; Malekzadeh A; Rezayat M; Ghazi-Khansari M
CORPORATE SOURCE: Department of Pharmacology, Tehran University of Medical Sciences, Iran.
SOURCE: Pharmacology & toxicology, (1995 Dec) 77 (6) 360-4. Journal code: 8702180. ISSN: 0901-9928.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19990129
Entered Medline: 19970124

AB In the present study, the effect of cholecystokinin agonists and antagonists on dependence to morphine in mice has been investigated. Mice were treated subcutaneously with morphine (50, 50 and 75 mg/kg) three times daily for 2-4 days, and a last dose of morphine (50 mg/kg) was administered on day 3, 4 or 5. Withdrawal syndrome (jumping) was precipitated by naloxone (2.5, 5 and 10 mg/kg) which was administered intraperitoneally 2 hr after the last dose of morphine. To study the effects of cholecystokinin receptor agonists or antagonists, 10 injection of morphine (3 administrations each day) for dependence and a dose of 5

mg/kg of naloxone for withdrawal induction were employed. Cholecystokinin-8 (0.001-0.01 mg/kg), low doses of the cholecystokinin agonists caerulein (0.00001 and 0.0001 mg/kg) and, unsulfated cholecystokinin (but not high doses) as well as the antagonists MK-329 (0.5-1 mg/kg) and L-365,260 (0.5-1 mg/kg) elicit reduction of the nalaxone-induced jumping. The inhibition of jumping induced by caerulein was reduced with the selective cholecystokinin antagonists MK-329 and L-365,260. It is concluded that cholecystokinin mechanism(s) may be involved in morphine dependence, that the agonists may act on a presynaptic receptors and that the antagonists may work on postsynaptic receptors.

CT Check Tags: Male
Animals
Benzodiazepinones: PD, pharmacology
Caerulein: PD, pharmacology
Cholecystokinin: AA, analogs & derivatives
Cholecystokinin: PD, pharmacology
Devazepide
Drug Interactions
Hormone Antagonists: PD, pharmacology
Injections, Subcutaneous
Mice
Morphine: AD, administration & dosage
Morphine: PD, pharmacology
*Morphine Dependence: DT, drug therapy
***Naloxone: PD, pharmacology**
*Narcotic Antagonists: PD, pharmacology
*Receptors, Cholecystokinin: AG, agonists
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Substance Withdrawal Syndrome

RN **103420-77-5 (Devazepide)**; 17650-98-5 (Caerulein); 465-65-6 (Naloxone); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Hormone Antagonists); 0 (Narcotic Antagonists); 0 (Receptors, Cholecystokinin)

L29 ANSWER 14 OF 124 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 95265138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7746354
TITLE: Cholecystokinin potentiates morphine anticonvulsant action through both CCK-A and CCK-B receptors.
AUTHOR: Legido A; Adler M W; Karkanias C; Geller E B; Bradley E; Greenstein J I; Grover W D
CORPORATE SOURCE: Department of Pediatrics, Temple University School of Medicine, Philadelphia, PA, USA.
CONTRACT NUMBER: DA 00376 (NIDA)
S07 RR05417 (NCRR)
SOURCE: Neuropeptides, (1995 Feb) 28 (2) 107-13.
Journal code: 8103156. ISSN: 0143-4179.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950621
Last Updated on STN: 19990129
Entered Medline: 19950614

AB Recent studies have suggested that cholecystokinin may have a role in modulating the effects of the endogenous opioid system in physiological functions such as thermoregulation and pain control. However, the

possible interaction of cholecystokinin and morphine in epileptogenesis is unknown. We studied the effect of subcutaneous morphine and intracerebroventricularly administered cholecystokinin octapeptide sulphate ester and receptor antagonists CCK-A (MK 329) and CCK-B (L 365,260) on seizures provoked by maximal electroshock in male Sprague-Dawley rats. Seizures were induced through electrode-gel-coated ear clip electrodes by a high voltage, high internal resistance constant current generator, 30 minutes after morphine administration and 10 minutes after cholecystokinin-8-SE, CCK-A and CCK-B infusion. Morphine decreased the length of the tonic component of the seizure and cholecystokinin potentiated this decrease. Cholecystokinin antagonists blocked the effects of both cholecystokinin and morphine. The results suggest that cholecystokinin acts as an endogenous agonist with opioids in the regulation of seizure susceptibility through both CCK-A and B receptors and may be responsible for part of the anticonvulsant action of morphine.

CT Check Tags: Male
Animals
*Benzodiazepinones: PD, pharmacology
*Cholecystokinin: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug
Injections, Spinal
***Morphine: PD, pharmacology**
*Phenylurea Compounds
Rats
Rats, Sprague-Dawley
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: DE, drug effects
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Seizures
Shock

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 15 OF 124 MEDLINE on STN DUPLICATE 20

ACCESSION NUMBER: 94272938 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8004452
TITLE: The CCKA receptor antagonist devazepide does not modify opioid self-administration or drug discrimination: comparison with the dopamine antagonist haloperidol.
AUTHOR: Higgins G A; Joharchi N; Wang Y; Corrigall W A; Sellers E M
CORPORATE SOURCE: Addiction Research Foundation, University of Toronto, Ont., Canada.
SOURCE: Brain research, (1994 Mar 21) 640 (1-2) 246-54. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 19990129
Entered Medline: 19940721

AB We previously reported that the selective cholecystokininA (CCKA) receptor antagonist, devazepide, blocked the acquisition of a morphine conditioned place preference (ref 28). An interpretation of this finding is that

devazepide may either affect an opioid discriminative stimulus and/or modify the rewarding properties of opioids. The present study was designed to investigate these issues by determining the effect of equivalent doses of devazepide in a morphine drug discrimination paradigm and a model of heroin self-administration. In each case, devazepide (0.001-1 mg/kg) was ineffective, i.e there was no antagonism of a morphine discriminative cue, and in a separate group of rats trained to self-administer heroin (0.03 mg/kg/infusion, FR5 schedule, 1h per day), devazepide did not alter the pattern of heroin responding. Because of evidence implicating an interaction between accumbens CCK and dopamine (DA) systems and evidence suggesting an apparent differential involvement of DA in opioid place conditioning, self-administration and drug discrimination behaviour, the effect of the DA antagonist haloperidol was examined in the latter two paradigms. In each test, haloperidol produced an effect inconsistent with a direct DAergic involvement. In a final study the CCKB antagonist L365-260 was also found not to affect an opioid discriminative cue. The present results therefore cast doubt on the potential utility of selective CCKA antagonists as treatments for opioid abuse, and further suggest that CCKB antagonists may not potentiate the subjective effects of opioids, an important finding considering that such drugs have been proposed as adjuncts to opioid therapy for the treatment of pain relief.

CT Check Tags: Comparative Study; Male
Animals
*Benzodiazepinones: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Cocaine: PD, pharmacology
Conditioning, Operant: DE, drug effects
Cues
Devazepide
*Discrimination (Psychology): DE, drug effects
*Dopamine Antagonists
Food
*Haloperidol: PD, pharmacology
Heroin: AD, administration & dosage
Heroin: PD, pharmacology
Morphine: AD, administration & dosage
Morphine: PD, pharmacology
Narcotics: AD, administration & dosage
***Narcotics: PD, pharmacology**
*Phenylurea Compounds
Rats
Rats, Wistar
*Receptors, Cholecystokinin: DE, drug effects
Self Administration: PX, psychology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 50-36-2 (Cocaine); 52-86-8 (Haloperidol); 561-27-3 (Heroin); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Dopamine Antagonists); 0 (Narcotics); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 16 OF 124 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 95120540 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7820614
TITLE: Cholecystokinin octapeptide (CCK-8) antagonizes morphine analgesia in nucleus accumbens of the rat via the CCK-B receptor.
AUTHOR: Pu S F; Zhuang H X; Han J S
CORPORATE SOURCE: Neuroscience Research Center, Beijing Medical University,

People's Republic of China.
CONTRACT NUMBER: DA 03983 (NIDA)
SOURCE: Brain research, (1994 Sep 19) 657 (1-2) 159-64.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19990129
Entered Medline: 19950214

AB The analgesic effect of systemic morphine (4 mg/kg, s.c.) was antagonized in a dose-dependent manner by cholecystokinin octapeptide (CCK-8) (0.1-0.5 ng) administered bilaterally to the nucleus accumbens of the rat. This effect of CCK-8 could be reversed by devazepide, a CCK-A receptor antagonist, at 50 ng and 200 ng and by L-365,260, a CCK-B receptor antagonist, at 5 ng administered bilaterally to the nucleus accumbens. A marked potentiation of morphine analgesia was achieved by intra-nucleus accumbens injection of 200 ng devazepide or 5 ng L-365,260. Since the effect of L-365,260 in antagonizing the anti-opioid effect of CCK-8 in the nucleus accumbens is 40 times more potent than devazepide, it is suggested that the anti-opioid effect of CCK-8 is mediated by CCK-B receptors. In conclusion, nucleus accumbens is a strategic site where CCK-8 exerts an anti-opioid activity, most probably via the CCK-B receptors.

CT Check Tags: Male
Animals
Benzodiazepinones: PD, pharmacology
Devazepide
Drug Synergism
Microinjections
***Morphine: AI, antagonists & inhibitors**
*Nucleus Accumbens: DE, drug effects
Nucleus Accumbens: ME, metabolism
*Phenylurea Compounds
Rats
Rats, Wistar
Receptor, Cholecystokinin B
*Receptors, Cholecystokinin: DE, drug effects
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 57-27-2 (Morphine)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 17 OF 124 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 94196376 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8146670
TITLE: Cholecystokinin octapeptide (CCK-8) antagonizes morphine analgesia in amygdala of the rat.
AUTHOR: Pu S F; Han J S
CORPORATE SOURCE: Department of Physiology, Beijing Medical University.
CONTRACT NUMBER: NIDA DA03983 (NIDA)
SOURCE: Sheng li xue bao [Acta physiologica Sinica], (1993 Oct) 45 (5) 470-8.
Journal code: 20730130R. ISSN: 0371-0874.
PUB. COUNTRY: China

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940511
Last Updated on STN: 20000303
Entered Medline: 19940429

AB CCK-8 administered bilaterally to the amygdala at 0.1-1.0 ng dose-dependently antagonized the analgesia induced by morphine (4 mg/kg, s. c.) as measured by the changes in tail flick latency (TFL). This effect of CCK-8 could be reversed by Devazepide, a CCK-A receptor antagonist dose-dependently at 50 ng and 200 ng, and by L-365, 260, a CCK-B receptor antagonist at 5 ng and 8 ng administered to the same site. The effect of morphine analgesia was potentiated by 200 ng Devazepide or 8 ng L-365, 260 administered bilaterally to amygdala. Devazepide and L-365, 260 per second showed no significant influence on basal TFL. The results indicate that amygdala is a strategic site where CCK-8 exerts an antiopioid activity. Since the effect of L-365, 260 was 25 times more potent than Devazepide, it suggests that the anti-opiod effect of CCK in amygdala is mediated by CCK-B receptors.

CT Check Tags: Male
*Amygdala: PH, physiology
Analgesia
Animals
Benzodiazepinones: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Devazepide
English Abstract
***Morphine: AI, antagonists & inhibitors**
*Phenylurea Compounds
Rats
Rats, Wistar
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 18 OF 124 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 94053864 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8235725
TITLE: Potentiation of morphine- and ohmefentanyl-induced analgesia by cholecystokinin receptor antagonists in rat.
AUTHOR: Zhou Y; Sun Y H; Han J S
CORPORATE SOURCE: Department of Physiology, Beijing Medical University.
CONTRACT NUMBER: NIDA DA 03983 (NIDA)
SOURCE: Sheng li xue bao [Acta physiologica Sinica], (1993 Jun) 45 (3) 255-61.
Journal code: 20730130R. ISSN: 0371-0874.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19990129

Entered Medline: 19931210

AB It has been reported that intrathecal (i.t.) injection of CCK-8 showed a marked antagonism to analgesic effects mediated by mu-opioid receptors in rat. The present study was performed to ascertain whether the blockade of endogenously released CCK-8 by potent and selective CCK-A antagonist devazepide and CCK-B antagonist L-365260 would affect opioid analgesia at the spinal cord level. A marked potentiation of the analgesic effect induced by morphine (4 mg/kg, sc) was produced by i.t. injection of 100 ng devazepide or 2.5 ng L-365260. Dose-response curves for the enhancement of the two drugs on morphine analgesia were bell-shaped. Intrathecal injection of 66 ng devazepide or 1.25 ng L-365260 was also shown to potentiate the analgesic effect induced by the selective mu-opioid agonist ohmefentanyl (OMF) (32 ng, i.t.). The dose-response curves were also bell-shaped. Devazepide or L-365260 per se produced no significant changes in rat tail flick latency (TFL). The above results are interpreted to mean that endogenously released CCK-8 in the spinal cord plays an antagonistic role to opioid analgesia, and it is the CCK-B receptors that mediate the anti-opioid effect since the dose of devazepide is 40-50 times higher than that of L-365260.

CT ***Analgesics: PD, pharmacology**
Animals
*Benzodiazepinones: PD, pharmacology
Devazepide
English Abstract
***Fentanyl: AA, analogs & derivatives**
Fentanyl: PD, pharmacology
***Morphine: PD, pharmacology**
*Pain Threshold: DE, drug effects
*Phenylurea Compounds
Rats
Rats, Wistar
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Spinal Cord: PH, physiology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 437-38-7 (Fentanyl); 57-27-2 (Morphine); 78995-14-9 (F 7302)

CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 19 OF 124 MEDLINE on STN DUPLICATE 24

ACCESSION NUMBER: 93245854 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8387008
TITLE: Increased release of immunoreactive cholecystokinin octapeptide by morphine and potentiation of mu-opioid analgesia by CCKB receptor antagonist L-365,260 in rat spinal cord.
AUTHOR: Zhou Y; Sun Y H; Zhang Z W; Han J S
CORPORATE SOURCE: Neuroscience Research Center, Beijing Medical University, People's Republic of China.
CONTRACT NUMBER: DA 03983 (NIDA)
SOURCE: European journal of pharmacology, (1993 Apr 6) 234 (2-3) 147-54.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306

ENTRY DATE: Entered STN: 19930618
Last Updated on STN: 19990129
Entered Medline: 19930603

AB This is the first report showing, in an in vivo study, that systemic morphine produced a marked (89%, P < 0.01) increase of the cholecystokinin octapeptide (CCK-8) immunoreactivity in the perfusate of the rat spinal cord, an effect completely reversed by naloxone. Since CCK-8 has been shown to possess potent anti-opioid activity at a spinal level, a blockade of the spinal cholecystokinin effect would be expected to potentiate opiate analgesia. With tail flick latency as a nociceptive index, it was found that intrathecal (i.t.) injection of a novel CCKB antagonist L-365,260 produced a marked potentiation of the analgesic effect induced by the mu-opioid agonists morphine (4 mg/kg s.c.) or ohmefentanyl (32 ng i.t.). Similar effects were obtained with the CCKA antagonist devazepide at a dose 40-50 times higher than that of L-365,260. Both devazepide and L-365,260 showed a bell-shaped dose-response curve. The results confirm the notion that an increased release of CCK-8 may constitute a self-limiting process for opioid effects at the spinal level, and that it is the CCKB receptor which mediates the anti-opioid effect of CCK-8 in the rat spinal cord.

CT Check Tags: Male
***Analgesia**
Analgesics: PD, pharmacology
Animals
*Benzodiazepinones: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug
Fentanyl: AA, analogs & derivatives
Fentanyl: PD, pharmacology
Injections, Spinal
Morphine: AI, antagonists & inhibitors
***Morphine: PD, pharmacology**
Naloxone: PD, pharmacology
Nociceptors: DE, drug effects
Pain Threshold: DE, drug effects
*Phenylurea Compounds
Radioimmunoassay
Rats
Rats, Wistar
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Opioid, mu: DE, drug effects
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Sincalide: IM, immunology
*Sincalide: ME, metabolism
Spinal Cord: DE, drug effects
*Spinal Cord: ME, metabolism
Subarachnoid Space: PH, physiology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 437-38-7 (Fentanyl); 465-65-6 (Naloxone); 57-27-2 (Morphine); 78995-14-9 (F 7302)

CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin); 0 (Receptors, Opioid, mu)

L29 ANSWER 20 OF 124 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 92305952 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1611514
TITLE: Morphine place conditioning is differentially affected by CCKA and CCKB receptor antagonists.

COMMENT: Erratum in: Brain Res 1992 May 29;581(2):359
AUTHOR: Higgins G A; Nguyen P; Sellers E M
CORPORATE SOURCE: Clinical Psychopharmacology Program, Addiction Research Foundation, Toronto, Ontario, Canada.
SOURCE: Brain research, (1992 Feb 14) 572 (1-2) 208-15.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 19990129
Entered Medline: 19920724

AB In the present study we have examined the interaction between the selective cholecystokinin (CCK)A and CCKB receptor antagonists, devazepide and L365-260 on morphine conditioned place preference (CPP). Using an unbiased procedure, morphine (1.5 mg/kg) produced a reliable CPP which was observed irrespective of the conditioning compartment type. Pretreatment with devazepide (0.001-0.01 mg/kg s.c.) produced a dose related attenuation of this response. At higher doses (0.1-1 mg/kg) this antagonism became variable and dependent on the training compartment with blockade only observed when conditioning was to the white/rough textured environment. This profile has also been reported for the serotonin (5-HT)3 receptor antagonist ondansetron. The CCKB antagonist L365-260 (0.000001-0.01 mg/kg) failed to antagonize the morphine CPP, if anything a mild potentiation was observed. To study this further we examined the interaction between L365-260 (0.01 mg/kg) and a subthreshold dose of morphine (0.3 mg/kg). At these doses neither drug elicited CPP, however when co-administered a significant CPP was recorded. Finally, L365-260 at 1 mg/kg induced a mild but significant CPP when administered alone. These results suggest a differential role of CCK receptor subtypes on reward-related behaviour and complement previous studies suggesting bimodal effects of CCK systems on mesolimbic dopamine function.

CT Check Tags: Comparative Study; Male
Animals
*Benzodiazepinones: PD, pharmacology
*Choice Behavior: DE, drug effects
*Conditioning, Operant: DE, drug effects
Devazepide
Morphine: AI, antagonists & inhibitors
***Morphine: PD, pharmacology**
Naloxone: PD, pharmacology
*Phenylurea Compounds
Rats
Rats, Inbred Strains
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Sodium Chloride: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 465-65-6 (Naloxone); 57-27-2 (Morphine); 7647-14-5 (Sodium Chloride)
CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 21 OF 124 MEDLINE on STN DUPLICATE 26
ACCESSION NUMBER: 92212521 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1557183
TITLE: The CCK-A and CCK-B receptor antagonists, devazepide and L-365,260, enhance morphine antinociception only in non-acclimated rats exposed to a novel environment.

AUTHOR: Lavigne G J; Millington W R; Mueller G P
CORPORATE SOURCE: Centre De Recherche en Sciences Neurologiques, Universite de Montreal, Canada.
CONTRACT NUMBER: DA04598 (NIDA)
SOURCE: Neuropeptides, (1992 Feb) 21 (2) 119-29.
Journal code: 8103156. ISSN: 0143-4179.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920515
Last Updated on STN: 19990129
Entered Medline: 19920501

AB Devazepide, a potent CCK-A receptor antagonist, and L-365,260, a selective CCK-B receptor antagonist, have been introduced as pharmacologic tools for differentiating the physiologic roles of CCK-A and CCK-B receptor subtypes. In the present study, we tested the effects of devazepide and L-365,260, on morphine antinociception in rats using the thermal sensorimotor tail flick test. Both devazepide and L-365,260 significantly enhanced the antinociceptive action of morphine, but only in rats that had not been acclimated to the laboratory environment or habituated to investigator handling. When tested with fully acclimated animals, devazepide and L-365,260 had no effect whatsoever; they neither enhanced nor attenuated morphine-induced antinociception. These observations indicate that the effects of devazepide and L-365,260, CCK antagonists, on morphine antinociception appear to be dependent on the animal's response to a new environment or to the stress induced by an unaccustomed experimental paradigm.

CT Check Tags: Male
*Adaptation, Physiological: PH, physiology
***Analgesia**
Animals
*Benzodiazepinones: PD, pharmacology
Devazepide
Environment
***Morphine**
Pain Measurement
*Phenylurea Compounds
Rats
Rats, Inbred Strains
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: PH, physiology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
Stress

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 57-27-2 (Morphine)
CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 22 OF 124 MEDLINE on STN DUPLICATE 27
ACCESSION NUMBER: 92159186 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1788334
TITLE: Antinociceptive and gastrointestinal transit effects of cholecystokinin (CCK-8) and related analogs of CCK-8 in the mouse.
AUTHOR: Ayres E A; Parkhurst D N; Fang S; Kramer T H; Hruby V J;

Burks T F
CORPORATE SOURCE: Department of Pharmacology, University of Arizona, Tucson 85724.
CONTRACT NUMBER: DA-02163 (NIDA)
DK-36289 (NIDDK)
SOURCE: Proceedings of the Western Pharmacology Society, (1991) 34 477-84.
Journal code: 7505899. ISSN: 0083-8969.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920410
Last Updated on STN: 19990129
Entered Medline: 19920320
CT Check Tags: Male
Amino Acid Sequence
***Analgesics: PD, pharmacology**
Animals
Benzodiazepinones: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: PD, pharmacology
Devazepide
Gastric Emptying: DE, drug effects
*Gastrointestinal Transit: DE, drug effects
Indoles: PD, pharmacology
Mice
Mice, Inbred ICR
Molecular Sequence Data
Morphinans: PD, pharmacology
Naloxone: PD, pharmacology
***Naltrexone**
***Naltrexone: AA, analogs & derivatives**
Narcotic Antagonists: PD, pharmacology
*Peptide Fragments: PD, pharmacology
Peptides: PD, pharmacology
*Phenylurea Compounds
Reaction Time: DE, drug effects
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, U.S. Gov't, P.H.S.
*Sincalide: AA, analogs & derivatives
Sincalide: PD, pharmacology
RN **103420-77-5 (Devazepide)**; 111555-53-4 (naltrindole); 118101-09-0 (L 365260); 129228-52-0 (SNF 8702); 137442-15-0 (SNF 8906); 16590-41-3 (Naltrexone); 25126-32-3 (Sincalide); 465-65-6 (Naloxone); 69344-77-0 (connective tissue-activating peptide); 9011-97-6 (Cholecystokinin)
CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Indoles); 0 (Morphinans); 0 (Narcotic Antagonists); 0 (Peptide Fragments); 0 (Peptides); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 23 OF 124 MEDLINE on STN DUPLICATE 28
ACCESSION NUMBER: 92008203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1915570
TITLE: Blockade of morphine place conditioning by the CCKA receptor antagonist devazepide.
AUTHOR: Higgins G A; Nguyen P; Sellers E M
CORPORATE SOURCE: Clinical Psychopharmacology Program, Addiction Research Foundation, Toronto, Ontario, Canada.

SOURCE: European journal of pharmacology, (1991 May 17) 197 (2-3) 229-30.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19990129
Entered Medline: 19911031

CT Check Tags: Male
Animals
*Benzodiazepinones: PD, pharmacology
*Conditioning (Psychology): DE, drug effects
Conditioning (Psychology): PH, physiology
Devazepide
***Morphine**
*Phenylurea Compounds
Rats
Rats, Inbred Strains
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: CL, classification
Receptors, Cholecystokinin: PH, physiology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 57-27-2 (Morphine)

CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 24 OF 124 MEDLINE on STN DUPLICATE 29

ACCESSION NUMBER: 91305409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1852780
TITLE: Influence of the selective cholecystokinin antagonist L-364,718 on pain threshold and morphine analgesia.
AUTHOR: Poggioli R; Vergoni A V; Sandrini M; Barbafiera L; Marrama D; Bertolini A
CORPORATE SOURCE: Institute of Pharmacology, University of Modena, Italy.
SOURCE: Pharmacology, (1991) 42 (4) 197-201.
Journal code: 0152016. ISSN: 0031-7012.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910908
Last Updated on STN: 19990129
Entered Medline: 19910822

AB The intracerebroventricular injection of the cholecystokinin-A receptor antagonist L-364,718, at the doses of 0.5, 5, 10 or 20 micrograms/mouse, while having no effect on pain threshold (hot plate, 51 degrees C), antagonized the analgesic activity of morphine (10 mg/kg i.p.). This effect was obtained with a dose of 10 micrograms/mouse and was associated with a reduction of brainstem opiate-binding sites.

CT Check Tags: Female; Male
***Analgesia**
Animals
Benzodiazepinones: ME, metabolism
*Benzodiazepinones: PD, pharmacology
Brain Stem: ME, metabolism

*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Mice
***Morphine**
Pain: DT, drug therapy
Pain: ME, metabolism
*Pain: PP, physiopathology
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Sensory Thresholds
RN **103420-77-5 (Devazepide)**; 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Receptors, Cholecystokinin)

L29 ANSWER 25 OF 124 MEDLINE on STN DUPLICATE 30
ACCESSION NUMBER: 91087152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2262899
TITLE: The cholecystokinin receptor antagonist devazepide enhances morphine-induced analgesia but not morphine-induced respiratory depression in the squirrel monkey.
AUTHOR: Dourish C T; O'Neill M F; Schaffer L W; Siegl P K; Iversen S D
CORPORATE SOURCE: Merck Sharp and Dohme Research Laboratories, Neuroscience Research Centre, Harlow, Essex, England.
SOURCE: Journal of pharmacology and experimental therapeutics, (1990 Dec) 255 (3) 1158-65.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19990129
Entered Medline: 19910207
AB The effects of the cholecystokinin antagonist devazepide on analgesia and respiratory depression induced by morphine in squirrel monkeys were examined. Pain thresholds were determined using the tail withdrawal procedure, in which monkeys restrained in chairs kept their tails in cool (35 degrees C) water for at least 20 sec, but withdrew them from warm (55 degrees C) water in less than 4 sec. Morphine produced a dose-related increase in tail withdrawal latencies from warm water. Devazepide (injected i.p. or p.o.) had no effect on tail withdrawal latencies when given alone but enhanced the analgesic effects of morphine. The devazepide dose-response curve for morphine enhancement was bell-shaped with doses of 3, 10, 30 and 100 micrograms/kg injected i.p. increasing morphine analgesia whereas higher and lower dose did not. In a separate group of monkeys, morphine produced dose-dependent decreases in respiratory rate and oxygen tension and increases in carbon dioxide tension. In contrast to its effects on morphine analgesia, devazepide had no effect on the various indices of morphine-induced respiratory depression. These data suggest that devazepide may have therapeutic utility as an adjuvant to morphine analgesia allowing lower dose of the opiate to be used to relieve pain and reducing the risk of opiate-induced respiratory depression.
CT Check Tags: Male
Administration, Oral
Analgesia
Animals
Benzodiazepinones: AD, administration & dosage

Benzodiazepinones: AE, adverse effects
*Benzodiazepinones: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Dose-Response Relationship, Drug
Drug Synergism
Injections, Intraperitoneal
Morphine: AE, adverse effects
***Morphine: PD, pharmacology**
Naloxone: PD, pharmacology
Pain: DT, drug therapy
Pain Measurement: MT, methods
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Respiration Disorders: CI, chemically induced
Saimiri
RN **103420-77-5 (Devazepide)**; 465-65-6 (Naloxone); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Receptors, Cholecystokinin)

L29 ANSWER 26 OF 124 MEDLINE on STN DUPLICATE 31
ACCESSION NUMBER: 90044651 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2812281
TITLE: Differential effects of the CCK antagonist, MK-329, on analgesia induced by morphine, social conflict (opioid) and defeat experience (non-opioid) in male mice.
AUTHOR: Hendrie C A; Shepherd J K; Rodgers R J
CORPORATE SOURCE: Department of Psychology, University of Bradford, England.
SOURCE: Neuropharmacology, (1989 Oct) 28 (10) 1025-32.
Journal code: 0236217. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19990129
Entered Medline: 19891213

AB The effects of the potent and selective CCK antagonist, MK-329, on morphine- and environmentally-induced analgesia were examined in male mice. The results show that MK-329 (0.005-0.1 mg/kg) was devoid of intrinsic analgetic activity on the mouse tail-flick assay and, over the dose range 0.01-0.5 mg/kg, was without significant effect upon non-opioid analgesia, induced by defeat experience. However, opposite effects of MK-329 on analgesia induced by morphine and opioid-mediated social conflict analgesia were observed. That is, 0.05-0.01 mg/kg MK-329 (but not smaller doses) enhanced, and modestly prolonged, the duration of analgesia induced by 5 mg/kg morphine. In direct contrast, 0.0001-0.5 mg/kg of the CCK antagonist very potently inhibited opioid-typical analgesia in mice exposed to intense conspecific attack. In the latter studies, a residual short-lasting analgesia in mice, treated with MK-329, was found to be resistant to naloxone (5 mg/kg), indicating its non-opioid nature and confirming the lack of effect of the CCK antagonist on opioid-independent analgesia. It is suggested that the variable effects of MK-329 on morphine-induced and opioid-mediated social conflict analgesia may reflect differential, dose-dependent effects at CCK-B and CCK-A sites respectively, a proposal consistent with the 500-fold potency difference observed between the two models.

CT Check Tags: Male
***Analgesia**

Animals
Behavior, Animal: DE, drug effects
*Benzodiazepinones: PD, pharmacology
*Conflict (Psychology)
Devazepide
Mice
Mice, Inbred DBA
***Morphine: PD, pharmacology**
Naloxone: PD, pharmacology
Nociceptors: DE, drug effects
Reaction Time: DE, drug effects
Research Support, Non-U.S. Gov't
*Sincalide: AI, antagonists & inhibitors
*Social Behavior
RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 465-65-6 (Naloxone); 57-27-2 (Morphine)
CN 0 (Benzodiazepinones)

L29 ANSWER 27 OF 124 MEDLINE on STN DUPLICATE 32
ACCESSION NUMBER: 89262552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2725851
TITLE: Morphine-induced analgesia in the rat paw pressure test is blocked by CCK and enhanced by the CCK antagonist MK-329.
AUTHOR: O'Neill M F; Dourish C T; Iversen S D
CORPORATE SOURCE: Merck Sharp and Dohme Research Laboratories, Neuroscience Research Centre, Harlow, Essex, U.K.
SOURCE: Neuropharmacology, (1989 Mar) 28 (3) 243-7.
Journal code: 0236217. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198907
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19990129
Entered Medline: 19890703
AB The effects of cholecystokinin octapeptide sulphated (CCK) and the potent CCK antagonist MK-329 (L-364, 718) on analgesia induced by morphine in the paw pressure test in the rat were examined. Both CCK (4-16 micrograms/kg) and MK-329 (0.1-8.0 mg/kg) had no significant effect on thresholds for pain when given alone, whereas morphine (2-16 mg/kg) induced dose-dependent analgesia. Cholecystokinin (4-16 micrograms/kg) abolished the analgesia induced by 8 mg/kg morphine. In contrast, doses of 1 and 2 mg/kg MK-329 enhanced the analgesia induced by 8 and 4 mg/kg morphine, respectively. The present data are consistent with previous reports that CCK blocks, and CCK antagonists enhance, opiate-induced analgesia in response to thermal pain stimuli. In addition, the results show that CCK/opiate interactions extend to mechanical pain stimuli. Recent ligand binding studies have shown that CCK receptors in the spinal cord of the rat (where CCK/opiate interactions are thought to occur) are predominantly of the CCK-B subtype. The drug MK-329 has a relatively weak (micromolar) affinity for CCK-B receptors and a high affinity (nanomolar) for CCK-A receptors. As relatively large doses (1-2 mg/kg) of MK-329 are required to enhance opiate-induced analgesia in the paw pressure test and tail flick test in rats it appears that CCK/opiate interactions in this species involve CCK-B receptors.
CT Check Tags: Male
Animals
*Benzodiazepinones: PD, pharmacology

Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug
Morphine: AI, antagonists & inhibitors
***Morphine: PD, pharmacology**
*Pain Measurement
Rats
Rats, Inbred Strains
Time Factors
RN **103420-77-5 (Devazepide)**; 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones)

L29 ANSWER 28 OF 124 MEDLINE on STN DUPLICATE 33
ACCESSION NUMBER: 88242689 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3378566
TITLE: Enhancement of morphine analgesia and prevention of morphine tolerance in the rat by the cholecystokinin antagonist L-364,718.
AUTHOR: Dourish C T; Hawley D; Iversen S D
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Harlow, Essex, U.K.
SOURCE: European journal of pharmacology, (1988 Mar 15) 147 (3) 469-72.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19880725
AB The potent and selective non-peptide cholecystokinin (CCK) antagonist L-364,718 (0.5-2.0 mg/kg s.c.) enhanced the analgesia induced by acute morphine treatment in the rat tail flick test. Chronic treatment with L-364,718 (1.0 mg/kg) prevented the development of tolerance to morphine analgesia (after a 6 day period of morphine treatment) but did not influence the onset of opioid dependence. Since L-364,718 is considerably more potent in inhibiting CCK binding to peripheral tissues than to brain membranes its interaction with morphine is surprising. The exact locus of this interaction, or whether it involves 'peripheral-type' (CCK-A) or 'central-type' (CCK-B) receptors is not known.
CT Check Tags: Male
***Analgesia**
Animals
*Benzodiazepinones: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Drug Interactions
*Drug Tolerance: DE, drug effects
***Morphine: PD, pharmacology**
Morphine Dependence
Rats
Rats, Inbred Strains
RN **103420-77-5 (Devazepide)**; 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones)

L29 ANSWER 29 OF 124 MEDLINE on STN DUPLICATE 34
ACCESSION NUMBER: 89091296 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3208830
TITLE: The novel CCK antagonist L364,718 abolished caerulein- but potentiates morphine-induced antinociception.
AUTHOR: Rattray M; Jordan C C; De Belleroche J
CORPORATE SOURCE: Department of Biochemistry, Charing Cross and Westminster Medical School, London, U.K.
SOURCE: European journal of pharmacology, (1988 Jul 26) 152 (1-2) 163-6.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19890223

AB The novel CCK antagonist L364,718 was tested on caerulein- and morphine-induced antinociception in rat using the paw pressure test. Caerulein-induced antinociception (ED50 = 30 micrograms/kg) was significantly inhibited by L354,718 (200 micrograms/kg i.p.) which on its own did not affect paw pressure threshold. In contrast, morphine-induced antinociception was significantly potentiated by L364,718. Since L364,718 is highly selective for 'peripheral' receptors which are found in tissue such as pancreas and gallbladder and a few discrete areas of brain, this receptor is likely to be implicated in the antinociceptive effect of caerulein.

CT Check Tags: Female
***Analgesics**
Animals
*Benzodiazepinones: PD, pharmacology
*Caerulein: AI, antagonists & inhibitors
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Drug Interactions
***Morphine: PD, pharmacology**
Pain: PP, physiopathology
Rats
Rats, Inbred Strains
Reaction Time: DE, drug effects
Research Support, Non-U.S. Gov't
Sensory Thresholds: DE, drug effects

RN **103420-77-5 (Devazepide)**; 17650-98-5 (Caerulein); 57-27-2 (Morphine); 9011-97-6 (Cholecystokinin)
CN 0 (Analgesics); 0 (Benzodiazepinones)

L29 ANSWER 30 OF 124 MEDLINE on STN
ACCESSION NUMBER: 2002462183 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12221244
TITLE: Dietary peptides induce satiety via cholecystokinin-A and peripheral opioid receptors in rats.
AUTHOR: Pupovac Jelena; Anderson G Harvey
CORPORATE SOURCE: Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, ON, Canada M5S 3E2.
SOURCE: Journal of nutrition, (2002 Sep) 132 (9) 2775-80.
Journal code: 0404243. ISSN: 0022-3166.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020911
Last Updated on STN: 20030207
Entered Medline: 20030206

AB We hypothesized that the digestion of proteins gives rise to peptides that initiate several satiety signals from the gut, and that the signals arising will be dependent on the protein source. The role of peripheral opioid and cholecystokinin (CCK)-A receptors was investigated. Casein, soy protein, and casein and soy hydrolysates were administered to rats by gavage (0.5 g protein/4 mL water). Food intake was measured over 2 h. The opioid receptor antagonist, naloxone methiodide (1.0 mg/kg) given intraperitoneally (i.p.), increased food intake when given at the same time as the hydrolysate preloads, 25 min after the casein preloads and 55 min after the soy protein preloads. The CCK-A receptor antagonist, devazepide (which reverses protein-induced food intake suppression), when given at 0.25 mg/kg, i.p., 60 min before preloads of each of three soy hydrolysates, also blocked suppression of food intake, but the strength and duration of the interaction depended on the preparation. When the two receptor antagonists were both administered with soy or casein preloads, their effects were additive. We conclude that peptides arising from digestion contribute to satiety by independent activation of both opioid and CCK-A receptors.

CT Check Tags: Male
Animals
Caseins: AD, administration & dosage
Caseins: ME, metabolism
Devazepide: PD, pharmacology
*Dietary Proteins: ME, metabolism
Digestion
Drug Interactions
Eating: DE, drug effects
Eating: PH, physiology
Hormone Antagonists: PD, pharmacology
Naloxone: PD, pharmacology
Narcotic Antagonists: PD, pharmacology
*Peptides: PH, physiology
Random Allocation
Rats
Rats, Wistar
Receptor, Cholecystokinin A
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: PH, physiology
Receptors, Opioid: AI, antagonists & inhibitors
*Receptors, Opioid: PH, physiology
Research Support, Non-U.S. Gov't
*Satiation: PH, physiology
Soybean Proteins: AD, administration & dosage
Soybean Proteins: ME, metabolism
Time Factors

RN **103420-77-5 (Devazepide)**; 465-65-6 (Naloxone)

CN 0 (Caseins); 0 (Dietary Proteins); 0 (Hormone Antagonists); 0 (Narcotic Antagonists); 0 (Peptides); 0 (Receptor, Cholecystokinin A); 0 (Receptors, Cholecystokinin); 0 (Receptors, Opioid); 0 (Soybean Proteins)

L29 ANSWER 31 OF 124 MEDLINE on STN

ACCESSION NUMBER: 2000075286 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10607394
TITLE: A locus and mechanism of action for associative morphine tolerance.
AUTHOR: Mitchell J M; Basbaum A I; Fields H L
CORPORATE SOURCE: Department of Physiology, University of California, San Francisco, San Francisco, California 94143-0444, USA.
CONTRACT NUMBER: DA 01949 (NIDA)
NS 21445 (NINDS)
SOURCE: Nature neuroscience, (2000 Jan) 3 (1) 47-53.
Journal code: 9809671. ISSN: 1097-6256.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB Repeated administration of an opioid in the presence of specific environmental cues can induce tolerance specific to that setting (associative tolerance). Prolonged or repeated administration of an opioid without consistent contextual pairing yields non-associative tolerance. Here we demonstrate that cholecystokinin acting at the cholecystokinin-B receptor is required for associative but not non-associative morphine tolerance. Morphine given in the morphine-associated context increased Fos-like immunoreactivity in the lateral amygdala and hippocampal area CA1. Microinjection of the cholecystokinin B antagonist L-365,260 into the amygdala blocked associative tolerance. These results indicate that cholecystokinin acting in the amygdala is necessary for associative tolerance to morphine's analgesic effect.

CT Check Tags: Male
Amygdala: DE, drug effects
Amygdala: ME, metabolism
Amygdala: PH, physiology
Animals
*Association Learning: DE, drug effects
Benzodiazepinones: AD, administration & dosage
Devazepide: PD, pharmacology
*Drug Tolerance: PH, physiology
Hippocampus: DE, drug effects
Hippocampus: ME, metabolism
Hippocampus: PH, physiology
Hormone Antagonists: PD, pharmacology
Immunohistochemistry
Microinjections
***Morphine: PD, pharmacology**
***Narcotics: PD, pharmacology**
Neurons: DE, drug effects
Neurons: ME, metabolism
Oncogene Proteins v-fos: ME, metabolism
Pain Measurement: DE, drug effects
Phenylurea Compounds: AD, administration & dosage
Rats
Rats, Sprague-Dawley
Receptor, Cholecystokinin A
Receptor, Cholecystokinin B
Receptors, Cholecystokinin: AI, antagonists & inhibitors

Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 57-27-2 (Morphine)
CN 0 (Benzodiazepinones); 0 (Hormone Antagonists); 0 (Narcotics); 0 (Oncogene Proteins v-fos); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin A); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 32 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1999431355 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10504030
TITLE: Relative blood-brain barrier permeabilities of the cholecystokinin receptor antagonists devazepide and A-65186 in rats.
AUTHOR: Woltman T A; Hulce M; Reidelberger R D
CORPORATE SOURCE: Department of Veteran's Affairs Medical Center, Omaha, NE 68105, USA.
CONTRACT NUMBER: DK52447 (NIDDK)
SOURCE: Journal of pharmacy and pharmacology, (1999 Aug) 51 (8) 917-20.
Journal code: 0376363. ISSN: 0022-3573.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991223

AB The blood-brain barrier permeabilities of the type-A cholecystokinin receptor antagonists devazepide and A-65186 (Nalpha-3-quinolinoyl-D-Glu-N,N-dipentylamide) have been compared with those of the reference compounds iodoantipyrine, which readily penetrates the blood-brain barrier, and mannitol, which does not. Anaesthetized rats received a bolus injection into the left carotid artery of [14C]iodoantipyrine (0.25 microCi) combined with [3H]mannitol, [3H]devazepide or [3H]A-65186 (1 microCi each). Rats were decapitated 12s after injection and the brains were removed. Four samples of left cerebrum (ca 100 mg each) were solubilized overnight and 14C and 3H activity were measured. The brain-uptake index for each test compound was determined as [(3H/14C for sample)]/[(3H/14C for injectate)] x 100, with a value of 100 representing blood-brain barrier permeability equal to that for iodoantipyrine. The brain-uptake index (mean+/-s.e.m.) was 1.6+/-0.3 for [3H]mannitol (n=5), 90.6+/-4.1 for [3H]devazepide (n=7, P<0.001 compared with mannitol) and 3.5+/-0.7 for [3H]A-65186 (n=4, P > 0.05 compared with mannitol, P < 0.001 compared with devazepide). Thus, devazepide readily penetrated the blood-brain barrier whereas A-65186 did not. It is concluded that devazepide and A-65186 are likely to be useful pharmacological tools for determining whether cholecystokinin is acting peripherally or at brain sites beyond the blood-brain barrier to produce satiety or any other function mediated by the type A cholecystokinin receptor.

CT Check Tags: Comparative Study; Male
Anesthesia
Animals
Antipyrine: AA, analogs & derivatives
Antipyrine: PK, pharmacokinetics
Antiviral Agents: PK, pharmacokinetics
*Blood-Brain Barrier: PH, physiology
Cerebellum: CH, chemistry

*Cerebellum: ME, metabolism
*Devazepide: PK, pharmacokinetics
Diuretics, Osmotic: PK, pharmacokinetics
*Hormone Antagonists: PK, pharmacokinetics
Mannitol: PK, pharmacokinetics
*Quinolines: PK, pharmacokinetics
Rats
Rats, Sprague-Dawley
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
RN **103420-77-5 (Devazepide)**; 119295-94-2 (A 65186); 129-81-7 (iodoantipyrine); 60-80-0 (Antipyrine); 69-65-8 (Mannitol)
CN 0 (Antiviral Agents); 0 (Diuretics, Osmotic); 0 (Hormone Antagonists); 0 (Quinolines); 0 (Receptors, Cholecystokinin)

L29 ANSWER 33 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1999325809 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10400222
TITLE: Anti-analgesia and reduced antinociception from supraspinally administered beta-endorphin in stressed rats: dependence on spinal cholecystokinin via cholecystokinin B receptors.
AUTHOR: Hawranko A A; Serafini M; Smith D J
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Robert C. Byrd Health Sciences Center of West Virginia University, Morgantown 26506, USA.
CONTRACT NUMBER: 2T32-GM07041 (NIGMS)
SOURCE: Neuroscience letters, (1999 May 28) 267 (2) 101-4. Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991215
AB Rats exposed to the stress of repeated exposure to a noxious heat source (52.5 degrees C, hot plate) exhibit stress-induced analgesia, but reduced antinociception (detected using the tail-flick test) to the administration of beta-endorphin into the periaqueductal gray region of the brain. This is accompanied by an anti-analgesic response (reduction in the stress-induced increase of tail flick latency) to doses of beta-endorphin (0.03 nmol) lower than those usually associated with antinociception. These alterations are prevented and antinociceptive potency is maintained when rats are treated with cholecystokinin (CCK) antagonists intrathecally. The potency of L-365,260 and L-364,718, selective CCK(B) and CCK(A) receptor antagonists, respectively, correlated with their apparent affinities for CCK(B) receptors, suggesting that the altered sensitivity to beta-endorphin is mediated via CCK(B) receptors.
CT Check Tags: Male
***Analgesia: MT, methods**
Animals
Benzodiazepinones: PD, pharmacology
*Cholecystokinin: PH, physiology
Devazepide: PD, pharmacology
*Heat Stress Disorders: PP, physiopathology
Hormone Antagonists: PD, pharmacology

Hyperalgesia: CI, chemically induced
Injections, Spinal
*Nociceptors: DE, drug effects
Nociceptors: PH, physiology
Phenylurea Compounds: PD, pharmacology
Rats
Rats, Sprague-Dawley
Receptor, Cholecystokinin B
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: PH, physiology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Stereoisomerism
*beta-Endorphin: AD, administration & dosage
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 60617-12-1 (beta-Endorphin); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Hormone Antagonists); 0 (Phenylurea Compounds); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 34 OF 124 MEDLINE on STN
ACCESSION NUMBER: 96368507 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8772515
TITLE: Effect of ethanol on cholecystokinin-stimulated zymogen conversion in pancreatic acinar cells.
AUTHOR: Katz M; Carangelo R; Miller L J; Gorelick F
CORPORATE SOURCE: Department of Medicine, West Haven Veterans Affairs Medical Center, Connecticut 06516, USA.
CONTRACT NUMBER: DK-07017 (NIDDK)
DK-32878 (NIDDK)
SOURCE: American journal of physiology, (1996 Jan) 270 (1 Pt 1) G171-5.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19990129
Entered Medline: 19961219

AB Exocrine pancreatic zymogens are proteolytically processed to active forms after they are secreted into the small intestine. However, intracellular conversion of zymogens to active forms can be stimulated by treating pancreatic acinar cells with high doses of cholecystokinin (0.1 microM) or carbamylcholine (0.1 mM). The high doses of cholecystokinin are unlikely to be achieved physiologically. The ability of ethanol to sensitize the acinar cell to zymogen conversion Induced by cholecystokinin or carbamylcholine was examined. Ethanol (10-200 mM) had no effect alone or when combined with carbamylcholine. However, ethanol (25 mM) added with low-dose cholecystokinin (0.1 nM) generated zymogen conversion that was 1) sixfold higher than cholecystokinin alone and 2) equivalent to that generated by highdose cholecystokinin (10 microM). The ability of ethanol to enhance cholecystokinin-induced zymogen conversion was dependent on the dose of ethanol and the duration of ethanol treatment. The cholecystokinin receptor antagonist, L-364,718, blocked the conversion stimulated by the addition of ethanol with cholecystokinin. This effect of ethanol did not change the affinity or number of cholecystokinin receptors, suggesting an effect more distal in the stimulus-activation cascade. These findings demonstrate that ethanol selectively sensitizes

the pancreatic acinar cell to cholecystokinin-stimulated zymogen proteolysis.

CT Check Tags: In Vitro; Male
Animals
Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Cholecystokinin: ME, metabolism
*Cholecystokinin: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug
Drug Synergism
*Enzyme Precursors: ME, metabolism
*Ethanol: PD, pharmacology
Hormone Antagonists: PD, pharmacology
Pancreas: CY, cytology
Pancreas: DE, drug effects
*Pancreas: ME, metabolism
Rats
Receptors, Cholecystokinin: ME, metabolism
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.

RN **103420-77-5 (Devazepide)**; 51-83-2 (Carbachol); 64-17-5 (Ethanol); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Enzyme Precursors); 0 (Hormone Antagonists); 0 (Receptors, Cholecystokinin)

L29 ANSWER 35 OF 124 MEDLINE on STN
ACCESSION NUMBER: 96383138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8791002
TITLE: Synergistic interactions between human transfected adenosine A1 receptors and endogenous cholecystokinin receptors in CHO cells.
AUTHOR: Dickenson J M; Hill S J
CORPORATE SOURCE: Department of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Nottingham, UK.. mqzjmd@mqnl.phpharm.nottingham.ac.uk
SOURCE: European journal of pharmacology, (1996 Apr 29) 302 (1-3) 141-51.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 20021218
Entered Medline: 19970206

AB The effect of Gi coupled receptor activation (adenosine A1 and 5-HT1B receptors) on cholecystokinin receptor-stimulated inositol phosphate accumulation has been investigated in Chinese hamster ovary cells transfected with the human adenosine A1 receptor cDNA (CHO-A1). CHO cells constitutively express the 5-HT1B receptor [Berg, Clarke, Sailstad, Saltzman and Maayani (1994) Mol. Pharmacol. 46, 477-484]. Our previous studies using CHO-A1 cells have revealed that both the adenosine A1 and 5-HT1B receptor are negatively coupled to adenylyl cyclase activity and stimulate increases in [Ca2+]i, through a pertussis toxin-sensitive pathway. In the present study the selective adenosine A1 receptor agonist N6-cyclopentyladenosine stimulated a pertussis toxin-sensitive increase in

total [3H]inositol phosphate accumulation. The sulphated C-terminal octapeptide of cholecystokinin (CCK-8) stimulated a robust and pertussis toxin-insensitive increase in [3H]inositol phosphate accumulation through the activation of CCKA receptors. Co-stimulation of CHO-A1 cells with N6-cyclopentyladenosine and CCK-8 produced a synergistic increase in [3H]inositol phosphate accumulation. The synergistic interaction between N6-cyclopentyladenosine and CCK-8 was abolished in pertussis toxin-treated cells. Synergy between N6-cyclopentyladenosine and CCK-8 still occurred in the absence of extracellular calcium. The 5-HT1B receptor agonist 5-carboxyamidotryptamine did not stimulate a measurable increase in [3H]inositol phosphate accumulation. Furthermore, 5-carboxyamidotryptamine had no significant effect on CCK-8 mediated [3H]inositol phosphate production. Activation of endogenous P2U receptors (Gq/G11 coupled) with ATP gamma S produced a significant increase in [3H]inositol phosphate accumulation. Co-stimulation of CHO-A1 cells with ATP gamma S and CCK-8 produced additive increases in [3H]inositol phosphate accumulation. These data indicate that CHO-A1 cells may prove a useful model system in which to investigate further the mechanisms underlying the intracellular 'cross-talk' between phospholipase C coupled receptors (Gq/G11 linked) and Gi/Go coupled receptors.

CT ***Adenosine: AA, analogs & derivatives**
Adenosine: AI, antagonists & inhibitors
Adenosine: PD, pharmacology
Adenylate Cyclase: AI, antagonists & inhibitors
*Adenylate Cyclase Toxin
Animals
Benzodiazepinones: PD, pharmacology
*CHO Cells: DE, drug effects
CHO Cells: ME, metabolism
Calcium: ME, metabolism
Devazepide
Dose-Response Relationship, Drug
Drug Synergism
Hamsters
Hormone Antagonists: PD, pharmacology
Humans
*Inositol Phosphates: ME, metabolism
*Pertussis Toxin
Proglumide: AA, analogs & derivatives
Proglumide: PD, pharmacology
*Receptors, Purinergic P1: ME, metabolism
Receptors, Purinergic P1: PH, physiology
*Receptors, Serotonin: ME, metabolism
Receptors, Serotonin: PH, physiology
Research Support, Non-U.S. Gov't
*Sincalide: PD, pharmacology
*Virulence Factors, Bordetella: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 41552-82-3 (N(6)-cyclopentyladenosine); 58-61-7 (Adenosine); 6620-60-6 (Proglumide); 7440-70-2 (Calcium); 97964-56-2 (lorglumide)

CN 0 (Adenylate Cyclase Toxin); 0 (Benzodiazepinones); 0 (Hormone Antagonists); 0 (Inositol Phosphates); 0 (Receptors, Purinergic P1); 0 (Receptors, Serotonin); 0 (Virulence Factors, Bordetella); EC 2.4.2.31 (Pertussis Toxin); EC 4.6.1.1 (Adenylate Cyclase)

L29 ANSWER 36 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95203041 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7895561
TITLE: Cholecystokinin is a potent protective agent against

alcohol-induced gastric injury in the rat. Role of endogenous prostaglandins.

AUTHOR: Mercer D W; Cross J M; Barreto J C; Strobel N H; Russell D H; Miller T A
CORPORATE SOURCE: Department of Surgery, University of Texas Medical School, Houston 77030.

CONTRACT NUMBER: DK 25838 (NIDDK)
SOURCE: Digestive diseases and sciences, (1995 Mar) 40 (3) 651-60. Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950504
Last Updated on STN: 19990129
Entered Medline: 19950421

AB Cholecystokinin is a gastrointestinal hormone known to physiologically regulate pancreatic protein secretion and gallbladder contractility. Some evidence suggests that cholecystokinin is also involved in the maintenance of gastrointestinal mucosal integrity. This study was undertaken to ascertain whether cholecystokinin could prevent the gastric mucosal injury induced by acidified ethanol and what role prostaglandins, and type A and type B cholecystokinin receptors might play in this process. Conscious, fasted rats were given subcutaneous saline or cholecystokinin octapeptide (10-100 micrograms/kg) 30 min before a 1-ml oral gastric bolus of acidified ethanol (150 mM HCl/50% ethanol). Five minutes later, rats were sacrificed and the total area of macroscopic injury quantitated (square millimeters). In additional experiments using a similar protocol, 1 ml of either the cyclooxygenase inhibitor, indomethacin (5 mg/kg), a type A cholecystokinin receptor antagonist, L-364,718 (0.01-1 mg/kg), or the type B cholecystokinin receptor antagonist, L-365,260 (12.5-25 mg/kg) was given intraperitoneally 30 min prior to pretreatment with cholecystokinin octapeptide. Cholecystokinin octapeptide dose-dependently prevented mucosal injury from acidified ethanol (corroborated by histology). The protective effect of cholecystokinin octapeptide was completely negated by L-364,718 and partially reversed by indomethacin, while L-365,260 had no discernible effect in this process. In a further study, cholecystokinin was unable to prevent the damaging effects of aspirin and the inhibition of endogenous prostaglandins. This, it appears that cholecystokinin is able to maintain mucosal integrity in the face of a damaging insult by activation of type A cholecystokinin receptors, an effect mediated, at least in part, through the release of endogenous prostaglandins.

CT Check Tags: Female
Animals
Aspirin: AE, adverse effects
Benzodiazepinones: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Devazepide
*Ethanol: AE, adverse effects
*Gastric Mucosa: DE, drug effects
Indomethacin: PD, pharmacology
*Phenylurea Compounds
Premedication
*Prostaglandins: PH, physiology
Rats
Rats, Sprague-Dawley
Receptor, Cholecystokinin A
Receptor, Cholecystokinin B

Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: PH, physiology
Research Support, U.S. Gov't, P.H.S.
Sincalide: PD, pharmacology
*Sincalide: PH, physiology
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 50-78-2 (Aspirin); 53-86-1 (Indomethacin); 64-17-5 (Ethanol); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Phenylurea Compounds); 0 (Prostaglandins); 0 (Receptor, Cholecystokinin A); 0 (Receptor, Cholecystokinin B); 0 (Receptors, Cholecystokinin)

L29 ANSWER 37 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95168318 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7864113
TITLE: Amazing pancreas: specific regulation of pancreatic secretion of individual digestive enzymes in rats.
AUTHOR: Maouyo D; Morisset J
CORPORATE SOURCE: Departement de Biologie, Faculte des sciences, Universite de Sherbrooke, Quebec, Canada.
SOURCE: American journal of physiology, (1995 Feb) 268 (2 Pt 1) E349-59.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950404
Last Updated on STN: 19990129
Entered Medline: 19950321

AB We investigated the effects of somatostatin (SMS)-201-995, atropine, and MK-329 on the role of cholinergic- and cholecystokinin-related systems and on the secretory relationship between five pancreatic digestive enzymes in rats. Animals kept in restraint cages and provided with pancreatic, biliary, duodenal, and jugular vein cannulas were treated as follows: 1) 0.25 micrograms.kg-1.h-1 caerulein alone, 2) both 0.25 micrograms.kg-1.h-1 caerulein and 100 micrograms.kg-1.h-1 atropine, 3) both caerulein and 5 micrograms.kg-1.h-1 SMS, 4) 91.3 micrograms.kg-1.h-1 carbachol alone, 5) both carbachol and 0.5 mg.kg-1.h-1 MK-329, and 6) both carbachol and 5 micrograms.kg-1.h-1 SMS, respectively. Food, but not water, was denied rats starting 10 h before the experiment and throughout the 6-h experimental period. The secretory patterns over the 6-h experimental period showed noticeably independent regulation of pancreatic secretion of individual digestive enzymes. The relationship between paired enzymes significantly varied according to the treatment. The correlation between chymotrypsinogen and the other enzymes was markedly modulated by MK-329. Our results suggest that SMS is a major "gate-keeper" in the regulation of exocrine pancreatic secretion and that the secretion of each digestive enzyme is individually regulated. Furthermore, they suggest that cholecystokinin and acetylcholine and their respective agonists are essentially initiators of secretory processes of the pancreas. Therefore, the paradigms of the regulation of pancreatic secretion heretofore accepted should be reexamined.

CT Check Tags: Comparative Study; Male
Animals
Atropine: PD, pharmacology
Benzodiazepinones: PD, pharmacology
Caerulein: PD, pharmacology

Carbachol: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Devazepide
*Digestion: PH, physiology
Octreotide: PD, pharmacology
*Pancreas: EN, enzymology
*Pancreas: PH, physiology
Pancreas: SE, secretion
Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
RN **103420-77-5 (Devazepide)**; 17650-98-5 (Caerulein); 51-55-8 (Atropine); 51-83-2 (Carbachol); 83150-76-9 (Octreotide); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones)

L29 ANSWER 38 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95258520 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7740050
TITLE: CCKA, but not CCKB, agonists suppress the hyperlocomotion induced by endogenous enkephalins, protected from enzymatic degradation by systemic RB 101.
AUTHOR: Dauge V; Corringer P J; Roques B P
CORPORATE SOURCE: Unite de Pharmacochimie Moleculaire et Structurale, U266 INSERM-URA D1500 CNRS, Universite Rene Descartes-UFR des Sciences Pharmaceutiques et Biologiques, Paris, France.
SOURCE: Pharmacology, biochemistry, and behavior, (1995 Feb) 50 (2) 133-9.
Journal code: 0367050. ISSN: 0091-3057.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
Last Updated on STN: 19990129
Entered Medline: 19950602

AB Interactions between CCKergic and enkephalinergic systems were studied in mice using behavioral responses measured in Animex. The hyperlocomotion induced by 5 mg/kg of RB 101, a mixed inhibitor of enkephalin-degrading enzymes able to cross the blood-brain barrier, was previously shown to be mediated by delta-opioid receptor stimulation. The IP administration of a CCKA agonist, Boc-Tyr-Lys-(CONH-o-tolyl)-Asp-Phe-NH2 (0.1, 1, 10 micrograms/kg), suppressed the hyperlocomotion produced by IV injection of 5 mg/kg of RB 101. The effect of the CCKA agonist was suppressed by a selective CCKA antagonist, devazepide, injected IP at doses of 20 and 200 micrograms/kg and was potentiated by the selective delta-opioid antagonist naltrindole at the doses of 0.03 mg/kg. IP injection of the selective CCKB agonist BC 264 (0.1-1 mg/kg) did not modify the RB 101-induced hyperlocomotor effect. These results reinforce the observed physiological antagonism between the endogenous CCK and opioid systems but are at variance with the responses measured in stressful conditions. It is concluded that CCKA, but not CCKB, receptor activation counteracts the opioid-related hyperlocomotion.

CT Check Tags: Male
Amino Acid Sequence
Animals
Benzodiazepinones: PD, pharmacology
*Cholecystokinin: AG, agonists

Cholecystokinin: AA, analogs & derivatives
Cholecystokinin: PD, pharmacology
Devazepide
*Disulfides: PD, pharmacology
*Enkephalins: PH, physiology
*Enzyme Inhibitors: PD, pharmacology
Mice
Molecular Sequence Data
*Motor Activity: DE, drug effects
Naltrexone: AA, analogs & derivatives
Naltrexone: PD, pharmacology
Narcotic Antagonists: PD, pharmacology
Peptide Fragments: PD, pharmacology
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
RN **103420-77-5 (Devazepide)**; 111555-53-4 (naltrindole); 135949-60-9 (RB 101); 16590-41-3 (Naltrexone); 63-91-2 (Phenylalanine); 9011-97-6 (Cholecystokinin)
CN 0 (BC 264); 0 (Benzodiazepinones); 0 (Disulfides); 0 (Enkephalins); 0 (Enzyme Inhibitors); 0 (Narcotic Antagonists); 0 (Peptide Fragments); 0 (Receptors, Cholecystokinin)

L29 ANSWER 39 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95396737 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7545293
TITLE: On the importance of cholecystokinin in neonatal pancreatic growth and secretory development in guinea pigs.
AUTHOR: Herrington M K; Joekel C S; Vanderhoof J A; Adrian T E
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, Nebraska, U.S.A.
CONTRACT NUMBER: 2-S07 RR05390-30 (NCRR)
SOURCE: Pancreas, (1995 Jul) 11 (1) 38-47.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 19990129
Entered Medline: 19951011

AB The role of cholecystokinin (CCK) in pancreatic growth and secretory development in fetal and neonatal guinea pigs was investigated by CCK receptor blockade. For the last 20 days of gestation, sows received the CCKA receptor antagonist, MK329 (25 nmol/kg/h) by continuous subcutaneous infusion. Alternatively, neonates from untreated females received an MK329 infusion for the first 4 or 15 days following birth. Pancreatic weight, DNA, RNA, protein, and amylase content per 100 g body weight and secretory responses to CCK, carbamylcholine, and phorbol ester were determined at birth and 4 days in animals receiving MK329 in utero and were measured at 4 and 15 days in neonatally infused animals. No significant changes in pancreatic growth parameters were seen in MK329-treated animals compared to controls, except for a small (14%; $p < 0.02$) decrease in weight after 15 days of neonatal exposure. Enhanced amylase secretion in response to CCK and carbamylcholine was seen in all groups receiving MK329 (all p values < 0.00001). Pancreatic growth and secretion were not inhibited by CCKA receptor blockade, which suggests

that the effects of CCK mediated by the CCKA receptor are not essential for growth or development of the pancreatic amylase secretory response in the neonatal guinea pig.

CT Check Tags: Female; Male
Amylases: SE, secretion
Animals
Animals, Newborn
Benzodiazepinones: AD, administration & dosage
*Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: BL, blood
*Cholecystokinin: PH, physiology
DNA: AN, analysis
Devazepide
Guinea Pigs
Injections, Subcutaneous
Organ Size
Pancreas: CH, chemistry
Pancreas: EM, embryology
*Pancreas: GD, growth & development
*Pancreas: SE, secretion
Phorbol Esters: PD, pharmacology
Pregnancy
Proteins: AN, analysis
RNA: AN, analysis
Random Allocation
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, U.S. Gov't, P.H.S.

RN **103420-77-5 (Devazepide)**; 51-83-2 (Carbachol); 63231-63-0 (RNA); 9007-49-2 (DNA); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Phorbol Esters); 0 (Proteins); 0 (Receptors, Cholecystokinin); EC 3.2.1.- (Amylases)

L29 ANSWER 40 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95088885 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7996417
TITLE: Role of endogenous cholecystokinin in the facilitation of mu-mediated antinociception by delta-opioid agonists.
AUTHOR: Noble F; Smadja C; Roques B P
CORPORATE SOURCE: Departement de Pharmacochimie Moleculaire et Structurale, U266 Institut National de la Sante et de la Recherche Medicale, Paris, France.
SOURCE: Journal of pharmacology and experimental therapeutics, (1994 Dec) 271 (3) 1127-34.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950126
Last Updated on STN: 20000303
Entered Medline: 19950117

AB Published results suggest that delta-opioid agonists can modulate the mu-mediated analgesia. In this work, the antinociceptive effects produced by the mu agonist [D-Ala2,NMe-Phe4,Gly-ol5]enkephalin or the mixed inhibitor of enkephalin-degrading enzymes RB 101 (N- [(R,S)-2-benzyl-3[(S)(2-amino-4-methyl- thio)butyldithio]-1-oxopropyl]-L-phenylalanine benzyl ester) were studied after administration of the systemically active

and selective delta agonist Tyr-D-Ser(O-tert-butyl)-Gly-Phe-Leu-Thr(O-tert-butyl). In the hot-plate test in mice, Tyr-D-Ser(O-tert-butyl)-Gly- Phe-Leu-Thr(O-tert-butyl) (i.v.) potentiated the antinociceptive responses elicited by [D-Ala2,NMe-Phe4,Gly-ol5]enkephalin (i.v.) or RB 101 (i.v.). These facilitatory effects were reversed not only by prior administration of the delta-selective antagonist naltrindole (0.5 mg/kg s.c.), but also unexpectedly by the selective cholecystokinin CCK-A antagonist MK-329 (20 micrograms/kg i.p.). In addition, the CCK analog [Boc- Tyr(SO3H)-Nle-Gly-Trp-Nle-Asp-Phe-NH2] (a mixed CCK-A/CCK-B agonist) increased the jump latency and this effect was blocked by MK-329 (20 micrograms/kg i.p.) and by naloxone, but not by the selective CCK-B antagonist L-365,260 (5 mg/kg i.p.). In contrast, the selective CCK-B agonist BC 264 (62 micrograms/kg i.v.) produced a hyperalgesic effect that was antagonized by L-365,260 (5 mg/kg i.p.). Taken together, these findings suggest that the potentiating effects of delta agonists on mu-mediated analgesia are due to an increase in the release of endogenous CCK interacting with CCK-A and CCK-B receptors and resulting in positive and negative regulation of the endogenous opioid system.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Male
Amino Acid Sequence
***Analgesia**
Animals
Benzodiazepinones: PD, pharmacology
Cholecystokinin: AA, analogs & derivatives
Cholecystokinin: PD, pharmacology
*Cholecystokinin: PH, physiology
Devazepide
Disulfides: PD, pharmacology
Enkephalin, Ala(2)-MePhe(4)-Gly(5)-
Enkephalins: PD, pharmacology
Mice
Molecular Sequence Data
Naloxone: PD, pharmacology
Naltrexone: AA, analogs & derivatives
Naltrexone: PD, pharmacology
*Oligopeptides: PD, pharmacology
Peptide Fragments: PD, pharmacology
Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Receptors, Opioid, delta: AG, agonists
*Receptors, Opioid, mu: PH, physiology
Sincalide: AA, analogs & derivatives
Sincalide: PD, pharmacology

RN 100929-53-1 (Enkephalin, Ala(2)-MePhe(4)-Gly(5)-); **103420-77-5 (Devazepide)**; 111035-57-5 (tyrosyl-seryl(O-t-butyl)-glycyl-phenylalanyl-leucyl-threonine(O-t-butyl)); 111555-53-4 (naltrindole); 135949-60-9 (RB 101); 16590-41-3 (Naltrexone); 25126-32-3 (Sincalide); 465-65-6 (Naloxone); 63-91-2 (Phenylalanine); 9011-97-6 (Cholecystokinin); 98640-66-5 (cholecystokinin (27-33), tert-butyloxycarbonyl-Nle(28,31)-)

CN 0 (BC 264); 0 (Benzodiazepinones); 0 (Disulfides); 0 (Enkephalins); 0 (Oligopeptides); 0 (Peptide Fragments); 0 (Receptors, Opioid, delta); 0 (Receptors, Opioid, mu)

L29 ANSWER 41 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95035112 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7524684
TITLE: Effects of cholecystokinin (CCK) and other secretagogues on isoforms of protein kinase C (PKC) in pancreatic acini.

AUTHOR: Pollo D A; Baldassare J J; Honda T; Henderson P A; Talkad V D; Gardner J D
CORPORATE SOURCE: Department of Internal Medicine, Saint Louis University Health Sciences Center, MO 63104.
SOURCE: Biochimica et biophysica acta, (1994 Oct 20) 1224 (1) 127-38.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19990129
Entered Medline: 19941207

AB We used rat pancreatic acini and measured the effects of various agents on digestive enzyme secretion, diacylglycerol (DAG) and the cellular distribution of protein kinase C (PKC) enzyme activity as well as isoforms of PKC determined by quantitative immunoblot analysis. TPA, but not CCK-8, caused translocation of PKC enzyme activity from the cytosol fraction to the membrane fraction. Immunoblot analysis detected PKC-alpha, PKC-delta, PKC-epsilon and PKC-zeta. PKC-beta, PKC-gamma and PKC-eta were not detected. TPA caused translocation of all isoforms from cytosol to membrane, whereas CCK-8 caused translocation of PKC-delta and PKC-epsilon, carbachol caused translocation of PKC-epsilon, and bombesin and secretin caused no detectable translocation of any isoform. Specific receptor antagonists could prevent, as well as reverse completely, the translocation of PKC isoforms caused by CCK-8 or carbachol. Agonists added in sequence with an interposed addition of a specific receptor antagonist caused cycling of PKC-epsilon between cytosol and membrane fractions. Each receptor-mediated agonist that caused translocation of PKC also increased DAG, and with CCK-8 and carbachol cycling of PKC-epsilon between cytosol and membrane was accompanied by corresponding cyclic changes in cellular DAG. CCK-JMV-180, bombesin and secretin increased DAG but did not cause translocation of any PKC isoform. Translocation of a PKC isoform could be accounted for by whether the increased DAG originated from PIP2 (accompanied by translocation) or from phosphatidylcholine (no accompanying translocation). Thus it appeared that DAG, in pancreatic acini, is functionally compartmentalized depending on the source of the lipid. Studies using CCK-8 and CCK-JMV-180 indicated that occupation of the low affinity state of the CCK receptor by either peptide increased DAG from phosphatidylcholine, whereas occupation of the very low affinity state by CCK-8 increased DAG from PIP2 and caused translocation of PKC-delta and PKC-epsilon. TPA stimulated amylase secretion, indicating that activation of PKC can stimulate enzyme secretion; however, with the various receptor-mediated secretagogues there was no consistent, unequivocal correlation between translocation of an isoform of PKC and accompanying changes in enzyme secretion.

CT Check Tags: Comparative Study; In Vitro
Amylases: SE, secretion
Animals
Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: PD, pharmacology
Devazepide
Diglycerides: ME, metabolism
Dose-Response Relationship, Drug
Enzyme Activation

Immunoblotting
*Isoenzymes: ME, metabolism
*Pancreas: DE, drug effects
Pancreas: EN, enzymology
Pancreas: ME, metabolism
*Protein Kinase C: ME, metabolism
Rats
Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: DE, drug effects
Sincalide: AA, analogs & derivatives
Sincalide: PD, pharmacology
Subcellular Fractions: DE, drug effects
Tetradecanoylphorbol Acetate: PD, pharmacology
RN **103420-77-5 (Devazepide)**; 119733-42-5 (JMV 180); 16561-29-8 (Tetradecanoylphorbol Acetate); 25126-32-3 (Sincalide); 51-83-2 (Carbachol); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Diglycerides); 0 (Isoenzymes); 0 (Receptors, Cholecystokinin); EC 2.7.1.37 (Protein Kinase C); EC 3.2.1.- (Amylases)

L29 ANSWER 42 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95035111 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7948036
TITLE: Biochemical regulation of the three different states of the cholecystokinin (CCK) receptor in pancreatic acini.
AUTHOR: Pandya P K; Huang S C; Talkad V D; Wank S A; Gardner J D
CORPORATE SOURCE: Department of Internal Medicine, Saint Louis University Health Sciences Center, MO 63104.
SOURCE: Biochimica et biophysica acta, (1994 Oct 20) 1224 (1) 117-26.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 20000303
Entered Medline: 19941207

AB We used rat pancreatic acini and measured binding of [125I]CCK-8 and [3H]L-364,718 to the three different states of the CCK receptor to examine potential biochemical regulation of ligand binding for each receptor state. Binding of [125I]CCK-8 to the high affinity state of the receptor was measured as carbachol-inhibitable binding of [125I]CCK-8, whereas binding of [125I]CCK-8 to the low affinity state was measured as carbachol-resistant binding of [125I]CCK-8. Interaction of CCK-8 with the very low affinity state of the CCK receptor was measured as CCK-8-inhibitable binding of [3H]L-364,718. [125I]CCK-8 that was bound to the high affinity state dissociated slowly at a rate of 0.20%/min and this dissociation was not altered by 30 mM NaF. Dissociation of [125I]CCK-8 bound to the low affinity state was biphasic--22% of the bound radioactivity dissociated completely within 3 min and the remaining 78% dissociated slowly at a rate of 0.19%/min. Dissociation of [125I]CCK-8 from the low affinity state was not altered by 30 mM NaF. The pattern of dissociation of bound [125I]CCK-8 from the pancreatic CCK receptor expressed in COS cells was also biphasic and closely resembled that observed in pancreatic acini. CCK-8 that was bound to the very low affinity state dissociated completely during a 20-min period of washing and resuspension of acini that had been first incubated with CCK-8. We

found extensive biochemical regulation of the different states of the CCK receptor in pancreatic acini. Bombesin, TPA, NaF, CCCP and trifluoperazine each altered binding of [125I]CCK-8 to the high affinity state and to the low affinity state, and except for bombesin each agent was more potent in affecting the high affinity state than the low affinity state. No agent tested affected the low affinity state but not the high affinity state. In contrast, a number of agents affected the high affinity state but not the low affinity state. These included receptor-mediated agonists (carbachol, secretin, VIP), 8Br-cAMP, NEM, agents that affect microtubules or microfilaments (cytochalasin B, vinblastine), calmodulin inhibitors (W-7, chlorpromazine) and genistein. Experiments with EGTA, A23187 and thapsigargin indicated that none of the three receptor states was influenced by intracellular or extracellular calcium. No agent tested altered the interaction of CCK-8 with the very low affinity state of the CCK receptor.(ABSTRACT TRUNCATED AT 400 WORDS)

CT Check Tags: Comparative Study; In Vitro
1-(5-Isoquinolinesulfonyl)-2-methylpiperazine
Animals
*Benzodiazepinones: ME, metabolism
Bombesin: PD, pharmacology
Carbachol
Cholecystokinin: ME, metabolism
Devazepide
GTP-Binding Proteins: ME, metabolism
Isoquinolines: PD, pharmacology
*Pancreas: ME, metabolism
Phosphorylation
Piperazines: PD, pharmacology
Rats
Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: ME, metabolism
Secretin: PD, pharmacology
*Sincalide: ME, metabolism
Sodium Fluoride: PD, pharmacology
Tetradecanoylphorbol Acetate: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 1393-25-5 (Secretin); 16561-29-8 (Tetradecanoylphorbol Acetate); 25126-32-3 (Sincalide); 31362-50-2 (Bombesin); 51-83-2 (Carbachol); 7681-49-4 (Sodium Fluoride); 84477-87-2 (1-(5-Isoquinolinesulfonyl)-2-methylpiperazine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Isoquinolines); 0 (Piperazines); 0 (Receptors, Cholecystokinin); EC 3.6.1.- (GTP-Binding Proteins)

L29 ANSWER 43 OF 124 MEDLINE on STN
ACCESSION NUMBER: 95035109 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7524683
TITLE: Characterization of the three different states of the cholecystokinin (CCK) receptor in pancreatic acini.
AUTHOR: Talkad V D; Patto R J; Metz D C; Turner R J; Fortune K P; Bhat S T; Gardner J D
CORPORATE SOURCE: Department of Internal Medicine, Saint Louis University, Health Sciences Center, MO 63104.
SOURCE: Biochimica et biophysica acta, (1994 Oct 20) 1224 (1) 103-16.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19990129
Entered Medline: 19941207

AB By measuring binding of [125I]CCK-8 and [3H]L-364,718 to rat pancreatic acini we demonstrated directly that the pancreatic CCK receptor can exist in three different affinity states with respect to CCK--high affinity, low affinity and very low affinity. Binding of [125I]CCK-8 reflects interaction of the tracer with the high and low affinity states, whereas binding of [3H]L-364,718 reflects interaction of the tracer with the low and very low affinity states. Treating acini with carbachol abolished the high affinity state of the CCK receptor and converted approximately 25% of the low affinity receptors to the very low affinity state. Carbachol treatment was particularly useful in establishing the values of Kd for the high and low affinity states for different CCK receptor agonists and antagonists. Of the various CCK receptor agonists tested, CCK-8 had the highest affinity for the high affinity state (Kd approximately 1 nM), whereas CCK-JMV-180 had the highest affinity for the low (Kd 7 nM) and very low affinity (Kd 200 nM) states. Gastrin and de(SO4)CCK-8 had affinities for the high and low affinity states of the receptor that were 100- to 400-fold less than those of CCK-8 but had affinities for the very low affinity state that were only 3- to 10-fold less than that of CCK-8. CCK receptor antagonists showed several patterns in interacting with the different states of the CCK receptor. L-364,718 had the same affinity for each state of the CCK receptor. CR1409 and Bt2cGMP each had similar affinities for the high and low affinity states and lower affinity for the very low affinity state. L-365,260 and CCK-JMV-179 had the highest affinity for the low affinity state and lower affinities for the high and very low affinity states. Different CCK receptor agonists caused the same maximal stimulation of amylase secretion but showed different degrees of amplification in terms of the relationship between their abilities to stimulate amylase secretion and their abilities to occupy the low affinity state of the CCK receptor. When amplification was expressed quantitatively as the value of Kd for the low affinity state divided by the corresponding EC50 for stimulating amylase secretion the values were CCK-8 (1000), de(SO)CCK-8 (1500), gastrin (100) and CCK-JMV-180 (Menozzi, D., Vinayek, R., Jensen, R.T. and Gardner, J.D. (1991) J. Biol. Chemical 266, 10385-1091).(ABSTRACT TRUNCATED AT 400 WORDS)

CT Check Tags: Comparative Study; In Vitro; Male
Amylases: SE, secretion
Animals
*Benzodiazepinones: ME, metabolism
Benzodiazepinones: PD, pharmacology
Carbachol
Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Dose-Response Relationship, Drug
Pancreas: DE, drug effects
*Pancreas: ME, metabolism
Pancreas: SE, secretion
Rats
Rats, Sprague-Dawley
Receptors, Cholecystokinin: AG, agonists
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: ME, metabolism
Research Support, Non-U.S. Gov't
Signal Transduction
*Sincalide: ME, metabolism

Sincalide: PD, pharmacology
RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 51-83-2 (Carbachol); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Receptors, Cholecystokinin); EC 3.2.1.- (Amylases)

L29 ANSWER 44 OF 124 MEDLINE on STN
ACCESSION NUMBER: 94151266 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7509060
TITLE: Characterization of a persistent inhibitory action of L-364,718 on cholecystokinin-stimulated enzyme secretion in pancreatic acini.
AUTHOR: Bhat S T; Talkad V D; Pollo D A; Gardner J D
CORPORATE SOURCE: Department of Internal Medicine, St. Louis University Medical Center, Missouri 63104.
SOURCE: Pancreas, (1994 Jan) 9 (1) 101-8.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19990129
Entered Medline: 19940318

AB Examining the actions of L-364,718 on rat pancreatic acini, we found that L-364,718 causes persistent inhibition of cholecystokinin (CCK)-8-stimulated enzyme secretion in acini that were first incubated with L-364,718, washed repeatedly, and then reincubated with CCK-8. This inhibition is maximal after as little as 5 s of first incubation with L-364,718, is unaltered by reducing the temperature of the first incubation from 37 to 4 degrees C and is specific for CCK-8 in that carbachol-stimulated enzyme secretion is unaltered. The inhibitory potency of L-364,718 added to the first incubation followed by washing and reincubation with CCK-8 is nearly the same as when L-364,718 is added together with CCK-8 in the same incubation. The persistent inhibitory action of L-364,718 is not attributable to residual free L-364,718 in the bulk phase of the second incubation medium. In addition, L-364,718 does not cause persistent inhibition by binding irreversibly to CCK receptors because the binding reaction is completely reversible and the persistent inhibition can be surmounted with appropriate concentrations of CCK-8. When acini are first incubated with L-364,718 and washed repeatedly, approximately 0.2% of the original L-364,718 remains trapped in a microenvironment within the acini. This trapping presumably results in a sufficiently high concentration of L-364,718 to produce its persistent, albeit surmountable inhibition.

CT Check Tags: Male
*Amylases: SE, secretion
Animals
Atropine: PD, pharmacology
Benzodiazepinones: ME, metabolism
*Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Kinetics
Pancreas: DE, drug effects
*Pancreas: EN, enzymology
Rats

Rats, Sprague-Dawley
Receptors, Cholecystokinin: ME, metabolism
*Sincalide: PD, pharmacology
RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 51-55-8 (Atropine); 51-83-2 (Carbachol); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Receptors, Cholecystokinin); EC 3.2.1.- (Amylases)

L29 ANSWER 45 OF 124 MEDLINE on STN
ACCESSION NUMBER: 93270050 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7684569
TITLE: Pancreatic acini possess endothelin receptors whose internalization is regulated by PLC-activating agents.
AUTHOR: Hildebrand P; Mrozinski J E Jr; Mantey S A; Patto R J; Jensen R T
CORPORATE SOURCE: Department of Gastroenterology, University Hospital, Basel, Switzerland.
SOURCE: American journal of physiology, (1993 May) 264 (5 Pt 1) G984-93.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930702
Last Updated on STN: 19990129
Entered Medline: 19930622

AB Endothelin-1 (ET-1) and ET-3 mRNA have been found in the pancreas. We investigated the ability of ET-1, ET-2, and ET-3 to interact with and alter dispersed rat pancreatic acinar cell function. Radiolabeled ETs bound in a time- and temperature-dependent fashion, which was specific and saturable. Analysis demonstrated two classes of receptors, one class (ETA receptor) had a high affinity for ET-1 but a low affinity for ET-3, and the other class (ETB receptor) had equally high affinities for ET-1 and ET-3. No specific receptor for ET-2 was identified. Pancreatic secretagogues that activate phospholipase C (PLC) inhibited binding of 125I-labeled ET-1 (125I-ET-1) or 125I-ET-3, whereas agents that act through adenosine 3',5'-cyclic monophosphate (cAMP) did not. A23187 had no effect on 125I-ET-1 or 125I-ET-3 binding, whereas the phorbol ester 12-O-tetradecanoylphorbol 13-acetate reduced binding. The effect of cholecystokinin octapeptide (CCK-8) was mediated through its own receptor. Stripping of surface bound ligand studies demonstrated that both 125I-labeled ET-1 and 125I-labeled ET-3 were rapidly internalized. CCK-8 decreased the internalization but did not change the amount of surface bound ligand. Endothelins neither stimulate nor alter changes in enzyme secretion, intracellular calcium, cAMP, or [3H]inositol trisphosphate (IP3). This study demonstrates the presence of ETA and ETB receptors on rat pancreatic acini; occupation of both receptors resulted in rapid internalization, which is regulated by PLC-activating secretagogues. Occupation of either ET receptor did not alter intracellular calcium, cAMP, IP3, or stimulate amylase release.

CT Check Tags: In Vitro; Male
1-Methyl-3-isobutylxanthine: PD, pharmacology
8-Bromo Cyclic Adenosine Monophosphate: PD, pharmacology
Amylases: SE, secretion
Animals
Benzodiazepinones: PD, pharmacology
Bombesin: PD, pharmacology

Calcimycin: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Cyclic AMP: ME, metabolism
Devazepide
*Endothelins: ME, metabolism
*Endothelins: PD, pharmacology
Enzyme Activation
Kinetics
Pancreas: CY, cytology
Pancreas: DE, drug effects
*Pancreas: ME, metabolism
*Phospholipase C: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptors, Endothelin: DE, drug effects
*Receptors, Endothelin: ME, metabolism
Research Support, Non-U.S. Gov't
Secretin: PD, pharmacology
Sincalide: PD, pharmacology
Tetradecanoylphorbol Acetate: PD, pharmacology
Vasoactive Intestinal Peptide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 1393-25-5 (Secretin); 16561-29-8 (Tetradecanoylphorbol Acetate); 23583-48-4 (8-Bromo Cyclic Adenosine Monophosphate); 25126-32-3 (Sincalide); 28822-58-4 (1-Methyl-3-isobutylxanthine); 31362-50-2 (Bombesin); 37221-79-7 (Vasoactive Intestinal Peptide); 51-83-2 (Carbachol); 52665-69-7 (Calcimycin); 60-92-4 (Cyclic AMP); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Endothelins); 0 (Receptors, Endothelin); EC 3.1.4.3 (Phospholipase C); EC 3.2.1.- (Amylases)

L29 ANSWER 46 OF 124 MEDLINE on STN
ACCESSION NUMBER: 93379229 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8369487
TITLE: Association of the peptidase inhibitor RB 101 and a CCK-B antagonist strongly enhances antinociceptive responses.
AUTHOR: Maldonado R; Derrien M; Noble F; Roques B P
CORPORATE SOURCE: Departement de Pharmacochomie Moleculaire et Structurale, INSERM U266-CNRS URA D1500, Universite Rene Descartes, Faculte des Sciences, Pharmaceutiques et Biologiques, Paris, France.
SOURCE: Neuroreport, (1993 Jul) 4 (7) 947-50.
Journal code: 9100935. ISSN: 0959-4965.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931029
Last Updated on STN: 19990129
Entered Medline: 19931008

AB The brain peptide cholecystokinin (CCK) has been shown to counteract the analgesic effects of morphine suggesting a physiological antagonism between opioid and CCK neural systems. This has been definitely demonstrated in this study by co-administration of the CCK-B selective antagonist L-365,260 with RB 101, a systemically active inhibitor of peptidases, which fully protects the endogenous opioids, the enkephalins, from their inactivation. The naloxone reversible analgesic effects induced by RB 101 in the mouse hot-plate and rat tail-flick tests were

strongly increased by low doses of L-365,260. These results could have important clinical applications by reducing the efficient dose of RB 101, which has recently been shown to be practically devoid of morphine-like side-effects.

CT Check Tags: Male
***Analgesics: PD, pharmacology**
Animals
Benzodiazepinones: PD, pharmacology
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
*Disulfides: PD, pharmacology
Drug Synergism
Mice
Pain Measurement: DE, drug effects
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Phenylurea Compounds
Rats
Rats, Sprague-Dawley
Reaction Time: DE, drug effects
Receptors, Cholecystokinin: AI, antagonists & inhibitors

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 135949-60-9 (RB 101); 63-91-2 (Phenylalanine); 9011-97-6 (Cholecystokinin)

CN 0 (Analgesics); 0 (Benzodiazepinones); 0 (Disulfides); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 47 OF 124 MEDLINE on STN
ACCESSION NUMBER: 94005444 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8401944
TITLE: Characterization of CCK receptors in a novel smooth muscle preparation from the guinea-pig stomach by use of the selective antagonists CI-988, L-365,260 and devazepide.
AUTHOR: Boyle S J; Tang K W; Woodruff G N; McKnight A T
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Addenbrookes Hospital Site, Cambridge.
SOURCE: British journal of pharmacology, (1993 Aug) 109 (4) 913-7. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19990129
Entered Medline: 19931102

AB 1. The cholecystokinin receptors mediating motor responses in a novel smooth muscle preparation from the corpus region of the guinea-pig stomach have been characterized by use of five agonist peptides and the antagonists CI-988, L-365,260 and devazepide. 2. Mucosa-denuded strips of circular muscle were contracted in a concentration-dependent manner by the five cholecystokinin (CCK)-related peptides CCK-8S, pentagastrin, gastrin-I, CCK-8US and CCK-4. 3. CI-988 was a powerful antagonist of the response to pentagastrin with an affinity (pKB = 9.49) similar to that obtained in CCKB receptor binding assays. With CCK-8S as the agonist, CI-988 was approximately 1000 fold less powerful as an antagonist. 4. Devazepide powerfully blocked responses to CCK-8S with an affinity (pKB = 9.54) that was in agreement with reported functional data obtained in pancreatic amylase secretion studies, a system exhibiting CCKA receptor activity. Devazepide displayed lower affinity against pentagastrin than

against CCK-8S. 5. CI-988 blocked responses to pentagastrin in an insurmountable manner in the presence of 3 nM devazepide; a concentration previously shown to block the CCKA receptor. The nature of the antagonism observed with L-365,260 was unaltered by the presence of devazepide. 6. The guinea-pig stomach corpus smooth muscle preparation contains both subtypes of CCK receptor and will be useful as a pharmacological tool for investigating the functional effects of novel CCK ligands.

CT Check Tags: In Vitro; Male
Animals
*Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: AA, analogs & derivatives
*Cholecystokinin: AI, antagonists & inhibitors
Cholecystokinin: PD, pharmacology
Devazepide
Gastric Mucosa: DE, drug effects
Gastric Mucosa: ME, metabolism
Gastrins: AI, antagonists & inhibitors
Gastrins: PD, pharmacology
Guinea Pigs
*Indoles: PD, pharmacology
*Meglumine: AA, analogs & derivatives
Meglumine: PD, pharmacology
Muscle Contraction: DE, drug effects
Muscle, Smooth: DE, drug effects
*Muscle, Smooth: ME, metabolism
*Phenylurea Compounds
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Receptors, Cholecystokinin: DE, drug effects
*Receptors, Cholecystokinin: ME, metabolism
Stomach: DE, drug effects
Stomach: ME, metabolism

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 130404-91-0 (PD 134308); 51-83-2 (Carbachol); 6284-40-8 (Meglumine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Gastrins); 0 (Indoles); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 48 OF 124 MEDLINE on STN
ACCESSION NUMBER: 93343321 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8342693
TITLE: Meal-induced c-fos expression in brain stem is not dependent on cholecystokinin release.
AUTHOR: Fraser K A; Davison J S
CORPORATE SOURCE: Department of Medical Physiology, University of Calgary, Alberta, Canada.
SOURCE: American journal of physiology, (1993 Jul) 265 (1 Pt 2) R235-9.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930917
Last Updated on STN: 19990129
Entered Medline: 19930827

AB Sprague-Dawley rats injected with a "physiological" dose of cholecystokinin octapeptide (CCK-8; 6 micrograms/kg ip) expressed c-fos

immunoreactivity in the nucleus of the tractus solitarius (NTS) and the area postrema (AP) of the brain stem. Injection of the CCK-A antagonist L-364,718 30 min before CCK-8 injection eliminated c-fos expression in these regions. These findings support the hypothesis that CCK-8 induced c-fos expression is mediated by CCK-A receptors. We then tested whether a meal (Isocal) could activate c-fos, and, if so, whether this response could be eliminated by L-364,718. Ingestion of Isocal induced c-fos immunoreactivity in the NTS and AP. Meal-induced c-fos expression was not blocked by the CCK-A antagonist L-364,718. These findings demonstrate for the first time that a purely physiological nonnoxious stimulus, a meal, induces c-fos in the rat brain stem and indicate that feeding induces c-fos expression by a pathway that is largely, if not entirely, independent of CCK release.

CT Animals
Benzodiazepinones: PD, pharmacology
*Brain Stem: ME, metabolism
Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: ME, metabolism
Devazepide
Dimethyl Sulfoxide: PD, pharmacology
*Eating
Medulla Oblongata: ME, metabolism
Proto-Oncogene Proteins c-fos: AI, antagonists & inhibitors
*Proto-Oncogene Proteins c-fos: ME, metabolism
Rats
Rats, Sprague-Dawley
Research Support, Non-U.S. Gov't
Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 67-68-5 (Dimethyl Sulfoxide); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Proto-Oncogene Proteins c-fos)

L29 ANSWER 49 OF 124 MEDLINE on STN

ACCESSION NUMBER: 94067584 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8247353
TITLE: Cholecystokinin-A but not cholecystokinin-B receptor stimulation induces endogenous opioid-dependent antinociceptive effects in the hot plate test in mice.
AUTHOR: Derrien M; Noble F; Maldonado R; Roques B P
CORPORATE SOURCE: Unite de Pharmacochimie Moleculaire et Structurale, U 266 INSERM-URA 1500 CNRS, Universite Rene Descartes, UFR des Sciences Pharmaceutiques et Biologiques, Paris, France.
SOURCE: Neuroscience letters, (1993 Oct 1) 160 (2) 193-6. Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19990129
Entered Medline: 19940104

AB The effects of intracerebroventricular administration of the cholecystokinin (CCK) analogue, BDNL, and the selective CCK-B agonist, BC 264, were determined using the hot plate test in mice. BDNL (0.2 nmol and 0.5 nmol) increased the jump and the paw lick latencies. These effects were blocked by the CCK-A antagonist MK-329 (0.02 mg/kg), supporting the involvement of CCK-A receptors in CCK-induced analgesia. In contrast, the selective CCK-B agonist BC 264 produced, at one dose (2.5 nmol), a slight

decrease in the lick latency that was only antagonized by the CCK-B antagonist. Naloxone, but not naltrindole, antagonized BDNL-induced analgesia. The results suggest that activation of CCK-A receptors by BDNL leads to antinociceptive responses indirectly mediated by stimulation of mu-opioid receptors by endogenous enkephalins.

CT Check Tags: Male
Animals
Benzodiazepinones: AD, administration & dosage
*Benzodiazepinones: PD, pharmacology
Cerebral Ventricles: DE, drug effects
*Cerebral Ventricles: PH, physiology
Cholecystokinin: AD, administration & dosage
*Cholecystokinin: AA, analogs & derivatives
Cholecystokinin: PD, pharmacology
Devazepide
Heat
Injections, Intraventricular
Mice
Mice, Inbred Strains
Naloxone: PD, pharmacology
*Pain: PP, physiopathology
Peptide Fragments: AD, administration & dosage
Peptide Fragments: PD, pharmacology
*Phenylurea Compounds
Receptors, Cholecystokinin: AI, antagonists & inhibitors
*Receptors, Cholecystokinin: PH, physiology
Research Support, Non-U.S. Gov't
Sincalide: AD, administration & dosage
Sincalide: AA, analogs & derivatives
Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 465-65-6 (Naloxone); 9011-97-6 (Cholecystokinin); 98640-66-5 (cholecystokinin (27-33), tert-butyloxycarbonyl-Nle(28,31)-)

CN 0 (BC 264); 0 (Benzodiazepinones); 0 (Peptide Fragments); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 50 OF 124 MEDLINE on STN
ACCESSION NUMBER: 93157899 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7679224
TITLE: Characterization of cholecystokinin receptors on the human gallbladder.
AUTHOR: Tokunaga Y; Cox K L; Coleman R; Concepcion W; Nakazato P; Esquivel C O
CORPORATE SOURCE: California Pacific Medical Center, San Francisco 94115.
SOURCE: Surgery, (1993 Feb) 113 (2) 155-62.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930326
Last Updated on STN: 19990129
Entered Medline: 19930308

AB BACKGROUND. Several studies examined in vivo and in vitro biologic activity of the human gallbladder in response to cholecystokinin (CCK). However, few studies have demonstrated directly the interaction of CCK with receptors on the human gallbladder, which is responsible for this biologic activity. METHODS. To characterize CCK receptors on human

gallbladder tissue, gallbladders were removed from human donor grafts that were being used for liver transplantation. The gallbladders were rapidly frozen and sectioned for measurement of binding of 125I-Bolton-Hunter-labeled-CCK-8 and were cut into strips for in vitro bioassay. RESULTS. Binding of 125I-BH-CCK-8 to human gallbladder was saturable, specific, and dependent on time, pH, and temperature. The binding was inhibited only by cholecystokinin-related peptides including CCK-8 (IC50 10 +/- 1.0 nmol/L) (mean +/- SD), des(SO3) CCK-8 (IC50 0.9 +/- 0.2 mumol/L), and gastrin-17-I (IC50 9.0 +/- 2.0 mumol/L) or specific CCK receptor antagonist L-364,718. Computer analysis of binding of 125I-BH-CCK-8 to gallbladder tissue showed a single class of binding sites with high affinity for CCK-8. Autoradiography localized binding of 125I-BH-CCK-8 only to the smooth muscle layer of the gallbladder. In the bioassay des(SO3) CCK-8 (EC50 1.2 +/- 0.7 mumol/L) and gastrin-17-I (EC50 4.5 +/- 2.4 mumol/L) were 150- and 563-fold less potent than CCK-8 (EC50 8.0 +/- 2.2 nmol/L). The relative potencies of CCK agonists for inhibiting binding of 125I-BH-CCK-8 agreed closely with their relative potencies for causing gallbladder contraction. The dose-response curve for CCK-8 alone to induce gallbladder contraction was not significantly different from those caused by CCK-8 plus 1 mumol/L tetrodotoxin or 1 mumol/L atropine. CONCLUSIONS. These results characterized the CCK receptors on smooth muscle of human gallbladder as sulfate dependent and causing gallbladder contraction.

CT Check Tags: In Vitro
Autoradiography
Benzodiazepinones: PD, pharmacology
Binding Sites
Carbachol: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug
Gallbladder: DE, drug effects
*Gallbladder: ME, metabolism
Gallbladder: PH, physiology
Gastrins: PD, pharmacology
Hormones: PD, pharmacology
Humans
Hydrogen-Ion Concentration
Iodine Radioisotopes: ME, metabolism
Muscle Contraction: DE, drug effects
*Muscle Contraction: PH, physiology
Muscle, Smooth: DE, drug effects
*Muscle, Smooth: ME, metabolism
Receptors, Cholecystokinin: DE, drug effects
*Receptors, Cholecystokinin: ME, metabolism
Reference Values
Secretin: PD, pharmacology
Serotonin: PD, pharmacology
Sincalide: AA, analogs & derivatives
Sincalide: PD, pharmacology
Substance P: PD, pharmacology
Temperature
Vasoactive Intestinal Peptide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 1393-25-5 (Secretin); 25126-32-3 (Sincalide); 25679-24-7 (desulfated sincalide); 33507-63-0 (Substance P); 37221-79-7 (Vasoactive Intestinal Peptide); 50-67-9 (Serotonin); 51-83-2 (Carbachol); 60748-06-3 (gastrin 17)

CN 0 (Benzodiazepinones); 0 (Gastrins); 0 (Hormones); 0 (Iodine Radioisotopes); 0 (Receptors, Cholecystokinin)

L29 ANSWER 51 OF 124 MEDLINE on STN

ACCESSION NUMBER: 92246980 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1575756
TITLE: Effects of CCK-8 on the cytoplasmic free calcium concentration in isolated rat islet cells.
AUTHOR: Fridolf T; Karlsson S; Ahren B
CORPORATE SOURCE: Department of Pharmacology, Lund University, Sweden.
SOURCE: Biochemical and biophysical research communications, (1992 Apr 30) 184 (2) 878-82.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19990129
Entered Medline: 19920602

AB The C-terminal octapeptide of cholecystokinin (CCK-8) is known to stimulate insulin secretion. We examined its effects on the cytoplasmic free calcium concentration ([Ca2+]IC) in isolated rat pancreatic islet cells. At 8.3 mM glucose and 1.28 mM Ca2+, CCK-8 (100 nM) rapidly increased [Ca2+]IC to a short-lived peak, whereafter the [Ca2+]IC, within 1.5 minutes, fell to values below baseline. CCK-8 also rapidly increased the [Ca2+]IC at 3.3 mM glucose and in a calcium deficient medium. However, either at low glucose or in the absence of extracellular Ca2+, the post-peak [Ca2+]IC did not fall below baseline levels. The CCKA receptor antagonist, L-364,718 (20 nM), inhibited the effects of CCK-8 on [Ca2+]IC. The results suggest that CCK-8 in islet cells liberates calcium from intracellular stores by activating CCKA receptors.

CT Check Tags: Male
Animals
Benzodiazepinones: PD, pharmacology
*Calcium: ME, metabolism
Carbachol: PD, pharmacology
Cells, Cultured
Cholecystokinin: AI, antagonists & inhibitors
*Cytoplasm: ME, metabolism
Devazepide
Egtazic Acid: PD, pharmacology
Fluorescent Dyes
Fura-2: AA, analogs & derivatives
Glucose: PD, pharmacology
Islets of Langerhans: DE, drug effects
*Islets of Langerhans: ME, metabolism
Kinetics
Rats
Rats, Inbred Strains
Research Support, Non-U.S. Gov't
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 105344-37-4 (fura-2-am); 25126-32-3 (Sincalide); 50-99-7 (Glucose); 51-83-2 (Carbachol); 67-42-5 (Egtazic Acid); 7440-70-2 (Calcium); 9011-97-6 (Cholecystokinin); 96314-98-6 (Fura-2)
CN 0 (Benzodiazepinones); 0 (Fluorescent Dyes)

L29 ANSWER 52 OF 124 MEDLINE on STN
ACCESSION NUMBER: 92359954 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1323276
TITLE: Influences of cholecystokinin octapeptide on

phosphoinositide turnover in neonatal-rat brain cells.
AUTHOR: Zhang L J; Lu X Y; Han J S
CORPORATE SOURCE: Neuroscience Research Center, Beijing Medical University, People's Republic of China.
CONTRACT NUMBER: DA 03983 (NIDA)
SOURCE: Biochemical journal, (1992 Aug 1) 285 (Pt 3) 847-50. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19920925
Last Updated on STN: 19990129
Entered Medline: 19920910

AB Cholecystokinin octapeptide (CCK-8) has been shown to be coupled to phosphoinositide turnover in pancreatic acini as well as in a kind of neuroblastoma cell and a human embryonic cell line. Little is known, however, about its link with phosphatidylinositol breakdown in the brain. The brains (minus cerebella) from 1-2-day-old neonatal rats were enzymically dissociated into single cells. The intact cells were prelabelled by incubation with myo-[3H]inositol for 3 h, and were then stimulated with agonists in the presence of 10 mM-LiCl. Carbachol at 1 mM induced an increase in InsP3 labelling in brain cells (peak at 30 min, and then a gradual decrease), and a static accumulation of InsP with time, whereas the labelling of InsP2 remained essentially unchanged. A very similar time-response curve was obtained for 10 nM-CCK-8 in stimulating phosphoinositide turnover. The dose-response curve for incubated brain cells revealed that the formation of InsP3 increased when the concentration of CCK-8 was increased from 0.1 to 10 nM. A further increase in CCK-8 concentration to 100-1000 nM resulted in a gradual decrease in InsP3 formation. InsP and InsP2 levels stayed relatively stable. The production of InsP3 stimulated by 10 nM-CCK-8 was dose-dependently suppressed by the CCK-A antagonist Devazepide in the concentration range 1-10 nM; the effect declined when the concentration was further increased to 100-1000 nM. In contrast, the CCK-B antagonist L365,260 showed a sustained suppression of InsP3 production at concentrations above 0.1 nM, i.e. in the range 1-1000 nM. The results provide evidence that CCK-8 stimulates the turnover of phosphoinositide and increases InsP3 labelling in dissociated neonatal-rat brain cells, in which both CCK-A and CCK-B receptors seem to be involved.

CT Animals
*Animals, Newborn: ME, metabolism
Benzodiazepinones: PD, pharmacology
Brain: DE, drug effects
*Brain: ME, metabolism
Carbachol: PD, pharmacology
Chlorides: PD, pharmacology
Devazepide
Kinetics
Lithium: PD, pharmacology
Lithium Chloride
*Phenylurea Compounds
*Phosphatidylinositols: ME, metabolism
Rats
Rats, Inbred Strains
Receptors, Cholecystokinin: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.

Sincalide: AI, antagonists & inhibitors
*Sincalide: PD, pharmacology
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 51-83-2 (Carbachol); 7439-93-2 (Lithium); 7447-41-8 (Lithium Chloride)
CN 0 (Benzodiazepinones); 0 (Chlorides); 0 (Phenylurea Compounds); 0 (Phosphatidylinositols); 0 (Receptors, Cholecystokinin)

L29 ANSWER 53 OF 124 MEDLINE on STN
ACCESSION NUMBER: 92204911 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1553366
TITLE: A pilot clinical trial of the cholecystokinin receptor antagonist MK-329 in patients with advanced pancreatic cancer.
AUTHOR: Abbruzzese J L; Gholson C F; Daugherty K; Larson E; DuBrow R; Berlin R; Levin B
CORPORATE SOURCE: Department of Medical Oncology, University of Texas M. D. Anderson Cancer Center, Houston 77030.
SOURCE: Pancreas, (1992) 7 (2) 165-71.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920509
Last Updated on STN: 19990129
Entered Medline: 19920428

AB MK-329 is a nonpeptidal, highly specific cholecystokinin (CCK) receptor antagonist, with affinity for pancreatic and gallbladder CCK receptors similar to CCK itself. MK-329 and its progenitor, asperlicin, can inhibit the growth of CCK receptor-positive human pancreatic cancer in athymic mice. Based on these activities and the ability of MK-329 to transiently increase food intake and enhance morphine analgesia in murine models, we conducted an open trial of MK-329 in 18 patients with advanced pancreatic cancer in whom the CCK receptor status of the tumors was unknown. Tumor response, pain control, and nutritional parameters (hunger rating, caloric intake, body weight, and anthropometrics) were serially assessed. The results of the study failed to demonstrate any impact of MK-329 on tumor progression, pain, or nutrition. Toxicity was mild and limited to nausea, vomiting, diarrhea, and abdominal cramps, with 17 of 18 patients able to tolerate treatment. While a role for MK-329 in the management of patients with advanced pancreatic cancer cannot be supported by the results of this trial, additional studies of this agent in patients with known CCK receptor-positive tumors, at escalated doses, and possibly in conjunction with other growth antagonists, appear warranted.

CT Check Tags: Female; Male
*Adenocarcinoma: DT, drug therapy
Adult
Aged
Analgesia
Benzodiazepinones: AE, adverse effects
*Benzodiazepinones: TU, therapeutic use
*Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Humans
Middle Aged
Nutrition

*Pancreatic Neoplasms: DT, drug therapy
*Receptors, Cholecystokinin: DE, drug effects
RN **103420-77-5 (Devazepide)**; 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones); 0 (Receptors, Cholecystokinin)

L29 ANSWER 54 OF 124 MEDLINE on STN
ACCESSION NUMBER: 92374087 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1354760
TITLE: L-365,260, a potent CCK-B/gastrin receptor antagonist, suppresses gastric acid secretion induced by histamine and bethanechol as well as pentagastrin in rats.
COMMENT: Erratum in: Jpn J Pharmacol 1992 Mar;58(3):329
AUTHOR: Nishida A; Yuki H; Tsutsumi R; Miyata K; Kamato T; Ito H; Yamano M; Honda K
CORPORATE SOURCE: Medicinal Research Laboratories I, Yamanouchi Pharmaceutical Co., Ltd., Ibaraki, Japan.
SOURCE: Japanese journal of pharmacology, (1992 Feb) 58 (2) 137-45. Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19921009
Last Updated on STN: 19990129
Entered Medline: 19920922

AB We evaluated the effects of a potent cholecystokinin (CCK)-B/gastrin receptor antagonist, L-365,260 (3R(+)-N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin - 3-yl)-N'-(3-methylphenyl) urea); a selective CCK-A receptor antagonist, devazepide (L-364,718); and cimetidine on gastric acid secretion induced by pentagastrin, histamine and bethanechol in anesthetized rats. We also evaluated the effects of L-365,260 and cimetidine on acid secretion in pylorus-ligated rats. Intravenous administration of L-365,260, L-364,718 and cimetidine dose-dependently reduced acid secretion induced by pentagastrin (20 nmol/kg/hr), with ED50 values of 0.63, 19.1 and 2.5 mumol/kg, respectively. Of interest was the finding that L-365,260, like cimetidine, dose-dependently inhibited acid secretion induced by histamine (100 mumol/kg/hr) and bethanechol (5 mumol/kg/hr) with ED50 values of 5.9 and 4.3 mumol/kg, respectively. L-364,718, even at 30 mumol/kg, i.v., had only a slight effect on histamine- or bethanechol-induced acid secretion. Gastric acid secretion was suppressed by treatment with L-365,260 (3-100 mumol/kg, i.v.) and cimetidine (11.9-396.4 mumol/kg, i.v.) in pylorus-ligated rats, with ED50 values of 13.3 and 96.9 mumol/kg, respectively. These results indicate that L-365,260 suppresses acid secretion induced by histamine and bethanechol in rats and that the gastrin receptor plays an important role in acid secretion in pylorus-ligated rats.

CT Check Tags: Comparative Study; Male
Animals
Benzodiazepinones: AD, administration & dosage
*Benzodiazepinones: PD, pharmacology
Bethanechol
Bethanechol Compounds: AD, administration & dosage
Bethanechol Compounds: PD, pharmacology
Cimetidine: AD, administration & dosage
Cimetidine: PD, pharmacology
Devazepide
Dose-Response Relationship, Drug

Gastric Acidity Determination
Gastric Mucosa: DE, drug effects
*Gastric Mucosa: SE, secretion
Histamine: AD, administration & dosage
Histamine: PD, pharmacology
Pentagastrin: AD, administration & dosage
Pentagastrin: PD, pharmacology
Perfusion
*Phenylurea Compounds
Rats
Rats, Inbred Strains
*Receptors, Cholecystokinin: AI, antagonists & inhibitors
RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 51-45-6 (Histamine); 51481-61-9 (Cimetidine); 5534-95-2 (Pentagastrin); 674-38-4 (Bethanechol)
CN 0 (Benzodiazepinones); 0 (Bethanechol Compounds); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 55 OF 124 MEDLINE on STN
ACCESSION NUMBER: 92052053 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1946314
TITLE: Role of cholecystokinin in cholestyramine-induced changes of the exocrine pancreas.
AUTHOR: Koop I; Lindenthal M; Schade M; Trautmann M; Adler G; Arnold R
CORPORATE SOURCE: Department of Internal Medicine, University of Marburg, F.R.G.
SOURCE: Pancreas, (1991 Sep) 6 (5) 564-70.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19990129
Entered Medline: 19911203
AB This study was an investigation of the role of cholecystokinin (CCK) in the stimulatory action of cholestyramine on rat exocrine pancreas. Postprandial CCK release was significantly enhanced by acute administration of cholestyramine (12.7 +/- 1.8 vs 3.7 +/- 0.5 pmol/L in controls). Over four weeks, rats were fed either regular diet or diet containing 6% cholestyramine, and were treated with the specific CCK receptor antagonist L-364,718 (2 x 0.5 mg/kg body weight/day s.c.) or DMSO (vehicle for the antagonist). Cholestyramine significantly increased pancreatic weight and trypsin and chymotrypsin contents. L-364,718 abolished these effects. Concomitant administration of antagonist and cholestyramine elevated amylase content, compared to controls. CCK levels in fasted animals did not differ between the four groups. The effect of the same dose of L-364,718 on pancreatic enzyme depletion, induced by the protease inhibitor camostate, was studied in a control experiment. A single dose of camostate (200 mg/kg) caused a 44-68% decrease in enzyme content. L-364,718 reversed this effect for all enzymes. We conclude that CCK is the mediator of cholestyramine-induced pancreatic hypertrophy and increase in content of proteases. After long-term administration, the CCK receptor antagonist, in combination with cholestyramine revealed an agonistic effect on individual, pancreatic enzyme content.
CT Check Tags: Male
Administration, Oral

Animals
Benzodiazepinones: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
Cholecystokinin: BL, blood
*Cholecystokinin: PH, physiology
Cholestyramine: AD, administration & dosage
*Cholestyramine: PD, pharmacology
Chymotrypsin: ME, metabolism
DNA: ME, metabolism
Devazepide
Dimethyl Sulfoxide: PD, pharmacology
Dose-Response Relationship, Drug
*Gabexate
*Gabexate: AA, analogs & derivatives
Guanidines: AE, adverse effects
Guanidines: PD, pharmacology
Hypertrophy: CI, chemically induced
Hypertrophy: ME, metabolism
Hypertrophy: PA, pathology
Organ Size: DE, drug effects
*Pancreas: DE, drug effects
Pancreas: EN, enzymology
Pancreas: PA, pathology
Rats
Rats, Inbred Strains
Receptors, Cholecystokinin: DE, drug effects
Research Support, Non-U.S. Gov't
Time Factors
Trypsin: ME, metabolism
Trypsin Inhibitors: AE, adverse effects
Trypsin Inhibitors: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 11041-12-6 (Cholestyramine); 39492-01-8 (Gabexate); 59721-28-7 (FOY 305); 67-68-5 (Dimethyl Sulfoxide); 9007-49-2 (DNA); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Guanidines); 0 (Receptors, Cholecystokinin); 0 (Trypsin Inhibitors); EC 3.4.21.1 (Chymotrypsin); EC 3.4.21.4 (Trypsin)

L29 ANSWER 56 OF 124 MEDLINE on STN
ACCESSION NUMBER: 91180815 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2008656
TITLE: Cerulein-induced pancreatitis in the ex vivo isolated perfused canine pancreas.
AUTHOR: Clemens J A; Olson J; Cameron J L
CORPORATE SOURCE: Department of Surgery, Johns Hopkins Medical Institutions, Baltimore, Md.
SOURCE: Surgery, (1991 Apr) 109 (4) 515-22.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19910519
Last Updated on STN: 19990129
Entered Medline: 19910430

AB Infusion of supramaximal doses of the cholecystokinin analog cerulein is well established as an in vivo technique for inducing experimental pancreatitis in small animals. An attempt was made to simulate this model and initiate pancreatitis in the ex vivo isolated perfused canine

pancreas. Control preparations gained minimal weight (mean 8.3 +/- 5.1 gm), demonstrated no edema accumulation, and did not develop hyperamylasemia (mean 1342 +/- 790 units) after 4 hours of perfusion. Electron microscopy after 4 hours of perfusion remained normal. Intraarterial cerulein infusion produced significant weight gain (mean 27.6 +/- 12.3 gm; p less than 0.001), edema formation, and marked hyperamylasemia (mean 26,838 +/- 21,341 units; p less than 0.001) after 4 hours of perfusion. During the 4-hour perfusion, electron microscopy of cerulein preparations demonstrated depletion of zymogen granules, condensing vacuole formation, and basolateral exocytosis. Pretreatment of cerulein preparations with the free radical scavengers superoxide dismutase and catalase and the iron chelator deferoxamine did not modify the pancreatitis. Continuous infusion of the nonpeptide cholecystokinin antagonist L364,718 reduced cerulein-induced weight gain (4.3 +/- 3.4 gm; p less than 0.001) and hyperamylasemia (9392 +/- 6718 units; p less than 0.05). We conclude that cerulein pancreatitis in the ex vivo isolated perfused canine pancreatic preparation is identical physiologically, biochemically, and morphologically with that seen in intact animals.

CT Check Tags: In Vitro
Acid-Base Equilibrium
Animals
Benzodiazepinones: PD, pharmacology
*Caerulein
Cholecystokinin: AI, antagonists & inhibitors
Devazepide
Dimethyl Sulfoxide: PD, pharmacology
Dogs
Endoplasmic Reticulum: UL, ultrastructure
Enzyme Precursors: UL, ultrastructure
Organ Size: DE, drug effects
*Pancreatitis: CI, chemically induced
Pancreatitis: PA, pathology
Reproducibility of Results

RN **103420-77-5 (Devazepide)**; 17650-98-5 (Caerulein); 67-68-5 (Dimethyl Sulfoxide); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Enzyme Precursors)

L29 ANSWER 57 OF 124 MEDLINE on STN

ACCESSION NUMBER: 91143812 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1996638
TITLE: Characterization of a gastrin-type receptor on rabbit gastric parietal cells using L365,260 and L364,718.
AUTHOR: Roche S; Bali J P; Galleyrand J C; Magous R
CORPORATE SOURCE: Laboratoire de Biochimie des Membranes, Centre National de la Recherche Scientifique UPR-8402, Institut National de la Sante et de la Recherche Medicale U249 Faculte de Pharmacie, Montpellier, France.
SOURCE: American journal of physiology, (1991 Feb) 260 (2 Pt 1) G182-8.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19990129
Entered Medline: 19910327

AB Previous studies have demonstrated that gastrin and the COOH-terminal

octapeptide of cholecystokinin (CCK-8) stimulated in vitro acid secretion from isolated rabbit gastric parietal cells. Both peptides bind to receptor sites located on these cells and induce an increase in phosphoinositide turnover and an uptake of [14C]aminopyrine ([14C]AP) with the same efficacy and potency. In the present study, we used the 3-(benzoylamino)-benzodiazepine analogue L365,260 and the 3-(acylamino)-benzodiazepine analogue L364,718 to investigate what type of receptor (gastrin type or CCK-A type) is involved in the regulation of the H+ secretory activity of the rabbit parietal cell. Neither L365,260 nor L364,718 alone caused stimulation of [3H]inositol phosphates ([3H]InsP) production. Each analogue inhibited 125I-labeled gastrin or 125I-CCK-8 binding to parietal cells and gastrin- or CCK-8-induced [3H]InsP production and [14C]AP accumulation. In all cases, L365,260 was approximately 70-100 times more potent than L364,718 (IC50 approximately 2-4 nM for L365,260 and approximately 0.2-0.4 microM for L364,718). Nevertheless, each antagonist displayed the same potency to inhibit the effects of gastrin or CCK-8. These results demonstrate that gastrin and CCK-8 interact with the same "gastrin-type" receptor on parietal cells. Moreover, L365,260 behaves as a competitive antagonist of the action of gastrin on parietal cells. Gastrin induces a rise in the levels of inositol 1,4,5-trisphosphate [Ins(1,4,5)P3] and inositol 1,3,4,5-tetrakisphosphate [Ins(1,3,4,5)P4] within the first seconds after parietal cell stimulation. The fact that L365,260 (10 nM) totally suppressed the gastrin-induced formation of Ins(1,4,5)P3 and Ins(1,3,4,5)P4 suggests the involvement of these isomers in the mediation of acid secretion through gastrin receptor activation.

CT Check Tags: In Vitro
Aminopyrine: ME, metabolism
Animals
*Benzodiazepinones: PD, pharmacology
Biological Transport: DE, drug effects
*Cholecystokinin: AI, antagonists & inhibitors
Chromatography, High Pressure Liquid
Devazepide
Gastrins: ME, metabolism
*Gastrins: PD, pharmacology
Inositol Phosphates: IP, isolation & purification
*Inositol Phosphates: ME, metabolism
Kinetics
*Parietal Cells, Gastric: ME, metabolism
*Phenylurea Compounds
Rabbits
Receptors, Cholecystokinin: DE, drug effects
*Receptors, Cholecystokinin: ME, metabolism
Research Support, Non-U.S. Gov't
*Sincalide: PD, pharmacology

RN **103420-77-5 (Devazepide)**; 118101-09-0 (L 365260); 25126-32-3 (Sincalide); 58-15-1 (Aminopyrine); 9011-97-6 (Cholecystokinin)

CN 0 (Benzodiazepinones); 0 (Gastrins); 0 (Inositol Phosphates); 0 (Phenylurea Compounds); 0 (Receptors, Cholecystokinin)

L29 ANSWER 58 OF 124 MEDLINE on STN
ACCESSION NUMBER: 91058406 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2244806
TITLE: Amelioration of cholinergic-induced pancreatitis with a selective cholecystokinin receptor antagonist.
AUTHOR: Bilchik A J; Zucker K A; Adrian T E; Modlin I M
CORPORATE SOURCE: Department of Surgery, Yale University School of Medicine, New Haven, Conn.

SOURCE: Archives of surgery (Chicago, Ill. : 1960), (1990 Dec) 125 (12) 1546-9.
Journal code: 9716528. ISSN: 0004-0010.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910222
Last Updated on STN: 19990129
Entered Medline: 19910102

AB Acute edematous pancreatitis follows excessive cholinergic stimulation in patients exposed to anticholinesterase-containing insecticides. We describe the role of cholecystokinin and the benefits of cholecystokinin receptor blockade in this form of pancreatitis. A cholinergic mimetic (carbachol) was administered to rats weighing 300 to 350 g and produced a form of edematous pancreatitis that mimics that seen in humans. Animals received carbachol intraperitoneally, either alone (250 micrograms/kg of body weight) or with cholecystokinin-receptor antagonist devazepide (3 mg/kg of body weight) and were killed 4 hours later. Carbachol administration resulted in a 19% increase in pancreatic weight, a fourfold increase in serum amylase levels, and a 14-fold increase in serum lipase levels. Plasma cholecystokinin levels, however, were not altered. Devazepide administered prior to cholinergic hyperstimulation blocked pancreatic weight increase and reduced elevations in serum amylase levels twofold and lipase levels fourfold. Although cholecystokinin levels are not elevated in this model of pancreatitis, blockade of even low, background concentrations of this regulatory peptide is beneficial.

CT Check Tags: Male
Acute Disease
Animals
*Benzodiazepinones: TU, therapeutic use
Carbachol
*Cholecystokinin: AI, antagonists & inhibitors
Cytoplasm: UL, ultrastructure
Devazepide
Endoplasmic Reticulum: UL, ultrastructure
Golgi Apparatus: UL, ultrastructure
Pancreatitis: CI, chemically induced
*Pancreatitis: DT, drug therapy
Pancreatitis: PA, pathology
Rats
Rats, Inbred Strains

RN **103420-77-5 (Devazepide)**; 51-83-2 (Carbachol); 9011-97-6 (Cholecystokinin)
CN 0 (Benzodiazepinones)

L29 ANSWER 59 OF 124 MEDLINE on STN
ACCESSION NUMBER: 90385190 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2402588
TITLE: Effects of cholecystokinin and cholinergic receptor blockade on guinea pig pepsinogen secretion.
AUTHOR: Basson M D; Adrian T E; Modlin I M
CORPORATE SOURCE: Gastrointestinal Surgery Research Group, Yale University, New Haven, CT.
SOURCE: Scandinavian journal of gastroenterology, (1990 Aug) 25 (8) 825-33.
Journal code: 0060105. ISSN: 0036-5521.
PUB. COUNTRY: Norway

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19990129
Entered Medline: 19901022

AB Although cholecystokinin (CCK) has been reported to stimulate pepsinogen secretion, this action has been poorly characterized. To assess the ability of CCK to regulate mammalian pepsinogen secretion, guinea pig fundic mucosa was incubated in Ussing chambers with CCK-8, carbamylcholine, and pentagastrin, and with cholinergic and CCK antagonists. CCK-8 stimulated pepsinogen secretion at 10(-10) M, with an ED50 of 10(-9) M and maximally (26-fold over basal) at 10(-8) M. Carbachol stimulated pepsinogen and acid secretion with an ED50 of 3 x 10(-7) M and maximally at 10(-6) M. Pentagastrin (10(-9) M-10(-6) M) did not affect acid or pepsinogen secretion, whereas gastrin-I (10(-6) M) stimulated acid secretion slightly but did not alter pepsinogen secretion. L364, 718 (10(-5) M), a specific CCK peripheral receptor antagonist, abolished all pepsigogic effects of 3 x 10(-9) M CCK-8 without altering basal acid or pepsinogen secretion or mucosal electric characteristics. L364,718-treated tissues unresponsive to CCK-8 nevertheless secreted pepsinogen and acid in response to 3 x 10(-7) M carbachol identically to control carbachol-treated preparations. Atropine (10(-5) M) blocked the response to 3 x 10(-7) M carbachol without inhibiting 10(-9) M CCK stimulation. These results support a specific receptor-mediated role for cholecystokinin in the physiologic regulation of guinea pig pepsinogen secretion.

CT Check Tags: Male
Animals
Atropine: PD, pharmacology
Benzodiazepinones: PD, pharmacology
Carbachol: PD, pharmacology
Cholecystokinin: AI, antagonists & inhibitors
*Cholecystokinin: PH, physiology
Cholinergic Antagonists
Devazepide
Gastric Mucosa: SE, secretion
Gastrins: PD, pharmacology
Guinea Pigs
Pentagastrin: PD, pharmacology
*Pepsinogens: SE, secretion
Receptors, Cholecystokinin: PH, physiology
*Receptors, Cholinergic: PH, physiology

RN **103420-77-5 (Devazepide)**; 51-55-8 (Atropine); 51-83-2 (Carbachol); 5534-95-2 (Pentagastrin); 9011-97-6 (Cholecystokinin); 9045-90-3 (gastrin I)

CN 0 (Benzodiazepinones); 0 (Cholinergic Antagonists); 0 (Gastrins); 0 (Pepsinogens); 0 (Receptors, Cholecystokinin); 0 (Receptors, Cholinergic)

L29 ANSWER 60 OF 124 MEDLINE on STN
ACCESSION NUMBER: 89336292 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2758237
TITLE: Cholecystokinin-octapeptide constricts guinea-pig and human airways.
AUTHOR: Stretton C D; Barnes P J
CORPORATE SOURCE: Department of Thoracic Medicine, National Heart and Lung Institute, London.
SOURCE: British journal of pharmacology, (1989 Jul) 97 (3) 675-82.

Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19990129
Entered Medline: 19890911

AB 1. Cholecystokinin-octapeptide (CCK-OP, 10(-10)-3 x 10(-6) M) produced a concentration-dependent contractile response in guinea-pig trachea which was enhanced by both the mechanical removal of the epithelium and by indomethacin (10(-5) M), with an EC50 of 6.18 +/- 0.10 x 10(-8) M. 2. Sub-threshold concentrations of CCK-OP, which did not alter the resting tone of the smooth muscle, did not alter responses produced to electrical field stimulation (EFS) or to vagal nerve stimulation in an intact tracheal tube preparation. Atropine (2 x 10(-6) M) did not alter the concentration-response curve to CCK-OP, indicating that CCK-OP contraction is not mediated by cholinergic mechanisms. 3. The inhibition of neutral endopeptidase (endopeptidase-24.11) by phosphoramidon (10(-5) M) gave a leftward shift in the CCK-OP concentration-response curve in tissues with intact epithelium obtained from normal animals, but had no effect in tissues denuded of epithelium or in tissues obtained from animals which had been actively sensitized and challenged with ovalbumin (OA). 4. CCK-OP-induced contractile responses were antagonized by the CCK-receptor antagonists dibutyryl cyclic guanosine monophosphate (pA2 = 4.3) and L-364,718 (pA2 = 9.6). 5. CCK-OP induced bronchoconstriction in large, but not small, human airways and was antagonized by the CCK-receptor antagonist L-364,718. CCK-OP had no effect on cholinergic neural responses elicited by EFS in human airways.

CT Check Tags: In Vitro; Male
Animals
Benzodiazepinones: PD, pharmacology
Bronchi: DE, drug effects
Devazepide
Electric Stimulation
Epithelium: PH, physiology
Glycopeptides: PD, pharmacology
Guinea Pigs
Humans
Indomethacin: PD, pharmacology
Muscle Contraction: DE, drug effects
Muscle, Smooth: DE, drug effects
Parasympathetic Nervous System: DE, drug effects
Research Support, Non-U.S. Gov't
Respiratory Hypersensitivity: PP, physiopathology
Sincalide: AI, antagonists & inhibitors
*Sincalide: PD, pharmacology
*Trachea: DE, drug effects

RN **103420-77-5 (Devazepide)**; 25126-32-3 (Sincalide); 36357-77-4 (phosphoramidon); 53-86-1 (Indomethacin)
CN 0 (Benzodiazepinones); 0 (Glycopeptides)

L29 ANSWER 61 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:113192 HCAPLUS
DOCUMENT NUMBER: 135:205338
TITLE: Different role of cholecystokinin (CCK)-A and CCK-B receptors in relapse to morphine dependence in rats
AUTHOR(S): Lu, L.; Huang, M.; Ma, L.; Li, J.

CORPORATE SOURCE: National Laboratory of Medical Neurobiology, Shanghai Medical University, Shanghai, 200032, Peop. Rep. China
SOURCE: Behavioural Brain Research (2001), 120(1), 105-110
CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The possible effects of different CCK receptor antagonists (MK-329 and L-365260) on the maintenance and reactivation of morphine conditioned place preference (CPP) were investigated in rats. Maintenance of morphine CPP could be induced by injection of morphine (10 mg/kg, s.c.), and this effect was attenuated by pretreatment with 1 but not by 0.1 mg L-365260/kg. Furthermore, following a 28-day extinction, the morphine CPP disappeared and then was reactivated again by a single injection of morphine (10 mg/kg). Pretreatment with L-365260 (1 and 0.1 mg/kg) blocked this reactivation of morphine CPP. In contrast, pretreatment with MK-329 (1 and 0.1 mg/kg) failed to do so. Thus, CCK-B receptors but not CCK-A receptors are involved in the maintenance and reactivation of morphine CPP. These findings suggest that CCK-B receptor antagonists might be of value in the treatment and prevention of relapse to drug dependence long after detoxification.

CC 1-11 (Pharmacology)

IT **57-27-2**, Morphine, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cholecystokinin-A and -B receptors role in relapse to morphine dependence)

IT **103420-77-5**, MK 329 118101-09-0, L 365260
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholecystokinin-A and -B receptors role in relapse to morphine dependence, as determined by response to)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 62 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:316267 HCAPLUS
DOCUMENT NUMBER: 133:114594
TITLE: Predicting blood-brain barrier permeation from three-dimensional molecular structure
AUTHOR(S): Crivori, Patrizia; Cruciani, Gabriele; Carrupt, Pierre-Alain; Testa, Bernard
CORPORATE SOURCE: Institute of Medicinal Chemistry, University of Lausanne, Lausanne-Dorigny, CH-1015, Switz.
SOURCE: Journal of Medicinal Chemistry (2000), 43(11), 2204-2216
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Predicting blood-brain barrier (BBB) permeation remains a challenge in drug design. Since it is impossible to determine exptl. the BBB partitioning of large nos. of preclin. candidates, alternative evaluation methods based on computerized models are desirable. The present study was conducted to demonstrate the value of descriptors derived from 3D mol. fields in estimating the BBB permeation of a large set of compds. and to produce a simple math. model suitable for external prediction. The method used (VolSurf) transforms 3D fields into descriptors and correlates them to the exptl.

permeation by a discriminant partial least squares procedure. The model obtained here correctly predicts more than 90% of the BBB permeation data. By quantifying the favorable and unfavorable contributions of physicochem. and structural properties, it also offers valuable insights for drug design, pharmacol. profiling, and screening. The computational procedure is fully automated and quite fast. The method thus appears as a valuable new tool in virtual screening where selection or prioritization of candidates is required from large collections of compds.

CC 1-3 (Pharmacology)

IT 50-22-6, Corticosterone 50-23-7, Cortisol 50-28-2, Estradiol, biological studies 50-47-5, Desipramine 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 51-61-6, Dopamine, biological studies 52-39-1, Aldosterone 52-86-8, Haloperidol 54-31-9 **57-27-2**, Morphine, biological studies 57-83-0, Progesterone, biological studies 58-00-4, Apomorphine 58-08-2, Caffeine, biological studies 58-22-0, Testosterone 58-39-9, Perphenazine 58-40-2, Promazine 58-73-1, Diphenhydramine 59-33-6, Mepyramine 59-92-7, Levodopa, biological studies 71-73-8 439-14-5, Diazepam 604-75-1, Oxazepam 1088-11-5, Nordazepam 4205-90-7, Clonidine 16590-41-3, Naltrexone 20290-10-2 22316-47-8, Clobazam 28797-61-7, Pirenzepine 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29122-68-7, Atenolol 29216-28-2, Mequitazine 30652-12-1, Cp21 30652-15-4, Cp24 30652-18-7, Cp25 34271-50-6 34391-04-3 34552-84-6, Isoxicam 36322-90-4, Piroxicam 51481-61-9, Cimetidine 51688-68-7 51742-87-1 **53179-11-6**, Loperamide 53230-10-7, Mefloquine 53772-82-0, cis-Flupentixol 53772-85-3, Trans-Flupentixol 57808-66-9, Domperidone 59429-50-4, Tamitinol 59804-37-4, Tenoxicam 66357-35-5, Ranitidine 67253-23-0 68844-77-9, Astemizole 69014-14-8, Tiotidine 69014-14-8D, Tiotidine, derivative 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71125-38-7, Meloxicam 71351-79-6, Icotidine 74011-58-8, Enoxacine 76210-47-4 76210-49-6 79660-72-3, Fleroxacin 79794-75-5, Loratadine 79794-75-5D, Loratadine, derivs. 82419-36-1, Ofloxacin 83903-06-4, Lupitidine 85721-33-1, Ciprofloxacin 86181-42-2, Temelastine 90729-42-3, Carebastine 90729-43-4, Ebastine 92998-17-9, S-Promethazine 98079-51-7 98106-17-3, Difloxacin 98323-83-2, Carmoxirole 101363-10-4, Rufloxacin **103420-77-5**, L 364718 **103420-82-2** 104076-38-2, Zolantidine 104076-38-2D, Zolantidine, deriv 110871-86-8, Sparfloxacin 112192-04-8, Roxindole 115900-75-9, Cp94 116003-91-9 118101-08-9 118101-09-0, L 365260 122384-14-9, L663581 123441-03-2, Rivastigmine 126055-13-8, Cp102 126588-96-3 126830-75-9 128246-10-6 130018-76-7 130018-77-8 130073-36-8 139965-10-9 139965-11-0 147368-41-0 148690-80-6 153205-46-0, EMD 61753 174635-78-0 174636-26-1 193222-55-8 285988-44-5 285988-45-6 285988-46-7 285988-47-8 285988-48-9 285988-49-0 285988-50-3 285988-51-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(blood-brain barrier permeation prediction from 3D mol. structure)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 63 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2000:246265 HCAPLUS

DOCUMENT NUMBER: 133:129756

TITLE: Cholecystokinin-B receptor antagonists attenuate morphine dependence and withdrawal in rats

AUTHOR(S): Lu, Lin; Huang, Mingsheng; Liu, Zhiyuan; Ma, Lan

CORPORATE SOURCE: Institute of Mental Health, West China University of

Medical Sciences, Chengdu, Peop. Rep. China
SOURCE: NeuroReport (2000), 11(4), 829-832
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The possible effect of a cholecystokinin-8 agonist (caerulein) and antagonists (MK-329 and L365,260) on the development of morphine dependence and withdrawal were investigated in rats. Caerulein treatment (0.01 and 0.1 mg/kg) increased the incidence of naloxone-induced withdrawal syndromes and delayed the extinction of morphine-conditioned place preference in morphine-dependent animals. The signs of the morphine withdrawal syndromes and the formation of morphine-conditioned place preference were suppressed by pretreatment with L365,260 (0.1 and 1 mg/kg) and not affected by pretreatment with MK-329 (0.1 and 1 mg/kg). The present study demonstrated CCK, acting on CCK-B receptors, participates in the development of the opiate dependence. These findings suggest that CCK-B receptor antagonists might be of some value in the treatment and prevention the relapse of opiate addicts.
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 4
IT **Opioids**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cholecystokinin-B receptor antagonists attenuate morphine dependence and withdrawal in rats)
IT **57-27-2**, Morphine, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cholecystokinin-B receptor antagonists attenuate morphine dependence and withdrawal in rats)
IT 17650-98-5, Caerulein **103420-77-5**, MK-329 118101-09-0, L365260
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin-B receptor antagonists attenuate morphine dependence and withdrawal in rats)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 64 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1999:45450 HCAPLUS
DOCUMENT NUMBER: 130:277056
TITLE: Effects of CCK antagonists on GABA mechanism-induced antinociception in the formalin test
AUTHOR(S): Rezayat, Mehdi; Tabarrai, Esmail; Parvini, Shirin; Zarrindast, Mohammad-Reza; Pirali, Morteza
CORPORATE SOURCE: School of Medicine, Department of Pharmacology, Tehran University of Medical Science, Tehran, Iran
SOURCE: European Neuropsychopharmacology (1999), 9(1-2), 9-14
CODEN: EURNE8; ISSN: 0924-977X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this work, the influences of CCK receptor antagonists on antinociception induced by the GABA receptor agonist, baclofen, and the GABA uptake inhibitor, THPO, in the formalin test have been studied. GABA-B agonist baclofen (0.75, 1.25 and 2.5 mg/kg), THPO, a GABA uptake inhibitor (1 and 2 mg/kg) and morphine (1.5, 3 and 6 mg/kg) induced antinociception in both phases of the formalin test in mice. The selective CCK receptor antagonists, L-365260, MK-329 (0.05, 0.125 and 0.25

mg/kg) and non-selective CCK receptor antagonist, proglumide (2.5, 5, 10 and 20 mg/kg) induced antinociception only in high doses. The CCK receptor antagonists potentiated baclofen (0.75, 1.25 and 2.5 mg/kg) or THPO (1 and 2 mg/kg) responses. It may be concluded that the CCK receptor mechanism may interact with GABA-function in its antinociceptive effect.

CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 1

IT **Analgesia**
Analgesics
(cholecystokinin receptor antagonists effect on GABAergic-induced antinociception in formalin test in mice)

IT 1134-47-0, Baclofen 6620-60-6, Proglumide 53602-00-9, THPO
103420-77-5, MK-329 118101-09-0, L-365260
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholecystokinin receptor antagonists effect on GABAergic-induced antinociception in formalin test in mice)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 65 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 1998:717528 HCAPLUS
DOCUMENT NUMBER: 130:61383
TITLE: Interactions between antinociception induced by cholecystokinin antagonists and GABA agonists in the tail-flick test
AUTHOR(S): Zarrindast, Mohammad-Reza; Rezayat, Mehdi; Ghanipoor, Nahid; Parvini, Shirin
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Tehran University of Medical Science, Tehran, 13145-784, Iran
SOURCE: Pharmacology & Toxicology (Copenhagen) (1998), 83(4), 143-148
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the study was to investigate the influences of cholecystokinin receptor antagonists L-365,260, MK-329 and proglumide on antinociception induced by baclofen and GABA uptake inhibitor 4,5,6,7-tetrahydroisoxazolo [4,5-c]pyridin-3-ol (THPO) in the tail flick test has been studied. Baclofen and THPO induced antinociception in the tail flick test. Morphine, and the CCK receptor antagonists, MK-329, L-365,260 and proglumide also induced antinociception. The CCK receptor antagonists potentiated antinociceptive response induced by both baclofen and THPO. It may be concluded that cholecystokinin receptor mechanism(s) may interact with antinociception induced by GABA receptor mechanism(s).

CC 2-6 (Mammalian Hormones)
ST cholecystokinin GABA receptor **analgesia**
IT **Analgesia**
(cholecystokinin antagonist effect on antinociception by GABA agonists in the tail-flick test)

IT **57-27-2**, Morphine, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholecystokinin antagonist effect on antinociception by GABA agonists in the tail-flick test)

IT 1134-47-0, Baclofen 6620-60-6, Proglumide 53602-00-9, THPO
103420-77-5, MK-329 118101-09-0, L-365260
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin antagonist effect on antinociception by GABA agonists in the tail-flick test)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 66 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 35
ACCESSION NUMBER: 1987:850 HCAPLUS
DOCUMENT NUMBER: 106:850
TITLE: A new simple mouse model for the in vivo evaluation of cholecystokinin (CCK) antagonists: comparative potencies and durations of action of nonpeptide antagonists
AUTHOR(S): Lotti, Victor J.; Cerino, Deborah J.; Kling, Paul J.; Chang, Raymond S. L.
CORPORATE SOURCE: Dep. Microb. Pharmacometrics, Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Life Sciences (1986), 39(18), 1631-8
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new simple mouse assay for the in vivo evaluation of CCK antagonists which is based upon visual determination of the gastric emptying of a charcoal meal is described. CCK-8 [25126-32-3] (24 μg/kg, s.c.) but not various other peptide and nonpeptide agents effectively inhibited gastric emptying in this test system. The effect of CCK-8 was antagonized by established peripheral CCK antagonists but not representative agents of various other pharmacol. classes. The rank order of potency of the CCK antagonists were: L-364718 [**103420-77-5**] (ED50 = 0.01 mg/kg, i.v.; 0.04 mg/kg, p.o.) > compound 16 [97964-56-2] (ED50 = 1.5 mg/kg i.v.; 2.0 m/kg p.o.) > asperlicin [93413-04-8] (ED50 = 14.8 mg/kg i.v.) > proglumide [6620-60-6] (ED50 = 184 mg/kg i.v.; 890 mg/kg, p.o.). Duration of action studies based upon ED50 values determined at various time intervals after oral administration showed that L-364,718 and proglumide are considerably longer acting than compound 16. Asperlicin (ED50 >300 mg/kg, p.o.) was ineffective as a CCK antagonist when administered orally. These data provide the first direct comparisons of the in vivo potencies of current CCK antagonists and demonstrate the utility of a new simple mouse assay for the in vivo characterization of peripheral CCK antagonists.
CC 2-6 (Mammalian Hormones)
IT 6620-60-6 93413-04-8 97964-56-2 **103420-77-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholecystokinin antagonist activity of, model for)
IT 50-67-9, Serotonin, biological studies 55-48-1, Atropine sulfate **57-27-2**, Morphine, biological studies 58-82-2 1393-25-5 1886-26-6, Norfenfluramine 5534-95-2, Pentagastrin 11000-17-2 11128-99-7 24305-27-9, TRH 25679-24-7 28797-61-7, Pirenzepine 31362-50-2 33507-63-0 37221-79-7, VIP 39379-15-2
RL: BIOL (Biological study)
(stomach emptying response to, cholecystokinin in relation to)

L29 ANSWER 67 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:409314 HCAPLUS
DOCUMENT NUMBER: 142:423880
TITLE: The use of non-opiates for the potentation of opiates
INVENTOR(S): Brew, John; Bannister, Robin Mark; Baxter, Andrew

Douglas; Rothaul, Alan; Lyne, Michael Harvey
PATENT ASSIGNEE(S): Arakis Ltd., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005041963	A1	20050512	WO 2004-GB4446	20041021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-24578 A 20031021
GB 2004-6657 A 20040324

AB A non-opioid **analgesic** is used for the treatment of intermittent or episodic pain experienced by a patient undergoing chronic pain treatment with an opioid **analgesic**.

IC ICM A61K031-445
ICS A61K031-395; A61K031-137; A61P029-00; A61P025-04; A61K031-165; A61K031-5513; A61K031-135; A61K031-381; A61K031-485
CC 1-11 (Pharmacology)
ST opiate **analgesic** chronic pain
IT **Analgesics**
Drug delivery systems
Human
Neoplasm
Osteoarthritis
Pain
Rheumatoid arthritis
(use of non-opiates for potentation of opiates)
IT **Opioids**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of non-opiates for potentation of opiates)
IT 6620-60-6, Proglumide 13669-70-0, Nefopam 23210-56-2, Ifenprodil **27203-92-5**, Tramadol 37148-27-9, Clenbuterol 93413-69-5, Venlafaxine **103420-77-5**, Devazepide 116539-59-4, Duloxetine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of non-opiates for potentation of opiates)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 68 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:825130 HCAPLUS
DOCUMENT NUMBER: 141:307586
TITLE: Method for the treatment of pain with opioid **analgesics** minimizing their side effects by

administration of devazepide
INVENTOR(S): Gibson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004198723	A1	20041007	US 2002-53962	20020122
US 2003139396	A1	20030724	US 2002-108659	20020327
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		
US 2004167146	A1	20040826	US 2003-622492	20030721
US 2004142959	A1	20040722	US 2004-752411	20040107

PRIORITY APPLN. INFO.:
GB 2002-1367 A 20020122
US 2002-53962 A2 20020122
US 2002-108659 A2 20020327
GB 2002-8129 A 20020409
US 2003-349431 A2 20030122

AB Method is disclosed for the treatment of a patient undergoing opioid **analgesic** therapy which comprises minimizing the side effects of the opioid by the administration of a therapeutically effective amount of devazepide.

IC ICM A61K031-5513
ICS A61K031-485
INCL 514221000; 514282000
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
ST opioid **analgesic** devazepide pain drug interaction
IT Intestine, disease
(constipation; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(inhalants; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(injections, i.m.; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(injections, i.v.; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(injections, s.c.; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(intranasal; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(intrathecal; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of

devazepide)
IT Blood
Dizziness
Drug interactions
Human
Pain
Vomiting
(method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT **Opioids**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Pain
(neuropathic; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT **Analgesics**
(opioid; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(oral; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(rectal; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Fatigue, biological
(tiredness and; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT Drug delivery systems
(transdermal, patch; method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT 52-26-6, Morphine hydrochloride **57-27-2**, Morphine, biological studies **57-42-1**, Pethidine **64-31-3**, Morphine sulphate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 468-10-0D, Morphinan, derivs. 469-62-5, Dextropropoxyphene 561-27-3, Heroin 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil **132875-61-7**, Remifentanil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)
IT **103420-77-5**, Devazepide **103420-82-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of pain with opioid **analgesics** minimizing their side effects by administration of devazepide)

L29 ANSWER 69 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:703123 HCAPLUS
DOCUMENT NUMBER: 141:167833
TITLE: Method of **analgesic** treatment by administration of devazepide
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S. Ser. No. 349,431.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167146	A1	20040826	US 2003-622492	20030721
US 2004198723	A1	20041007	US 2002-53962	20020122
US 2003139396	A1	20030724	US 2002-108659	20020327
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		

PRIORITY APPLN. INFO.:

US 2002-53962	B2	20020122
US 2002-108659	A2	20020327
GB 2002-8129	A	20020409
US 2003-349431	A2	20030122

AB A method of treating a patient undergoing **analgesic** therapy which comprises the sep., simultaneous or sequential administration of a therapeutically effective amount of an **analgesic** and an **analgesic** sparing amount of devazepide. There is also described the use of devazepide in the manufacture of a medicament which reduces the dose required for administration of an opioid **analgesic** and superpotentiates the effect of the **analgesic**.

IC ICM A61K031-485
INCL 514282000
CC 1-11 (Pharmacology)
Section cross-reference(s): 9
ST opioid devazepide **analgesic** therapy human
IT Drug delivery systems
(infusions, i.v.; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(infusions; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(inhalants; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(injections, i.m.; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(injections, i.v.; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(injections, s.c.; method of **analgesic** treatment by administration of devazepide)
IT Drug delivery systems
(intrathecal, intra-arterial; method of **analgesic** treatment by administration of devazepide)

IT **Analgesics**
Combination chemotherapy
Human
(method of **analgesic** treatment by administration of devazepide)

IT **Opioids**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of **analgesic** treatment by administration of devazepide)

IT Drug delivery systems
(nasal; method of **analgesic** treatment by administration of devazepide)

IT Drug delivery systems
(oral; method of **analgesic** treatment by administration of devazepide)

IT Drug delivery systems
(rectal; method of **analgesic** treatment by administration of devazepide)

IT Drug delivery systems
(transdermal; method of **analgesic** treatment by administration of devazepide)

IT 561-27-3, Diamorphine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Heroin; method of **analgesic** treatment by administration of devazepide)

IT **57-42-1**, Meperidine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Pethidine; method of **analgesic** treatment by administration of devazepide)

IT 52-26-6 **57-27-2**, Morphine, biological studies **64-31-3**, Morphine sulfate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 103-90-2, Paracetamol **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 915-30-0, Diphenoxylate **15307-86-5**, Diclofenac 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol 67889-72-9, Co-Codamol **71195-58-9**, Alfentanil **132875-61-7**, Remifentanil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of **analgesic** treatment by administration of devazepide)

IT **103420-77-5**, Devazepide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of **analgesic** treatment by administration of devazepide)

L29 ANSWER 70 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:392318 HCAPLUS
DOCUMENT NUMBER: 140:400077

TITLE: Pharmaceutical combinations including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and their use in treating gastrointestinal and abdominal visceral disorders
INVENTOR(S): Billstein, Stephan Anthony; Dumovic, Peter; Franco, Nicola; Iwicki, Mark Thomas; Pfannkuche, Hans-Jurgen; Wilusz, Edward Joseph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 722,784, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004092511	A1	20040513	US 2003-702688		20031106
PRIORITY APPLN. INFO.:			US 1999-266333P	P	19991210
			US 2000-722784	B1	20001127

AB The invention discloses a combination of a first agent including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and pharmaceutical compns. and formulations containing the combination. The invention also discloses a method for treating a gastrointestinal and abdominal visceral disorder by administering the pharmaceutical compns. to a patient. The pharmaceutical compns. may also be employed as laxatives, to prepare a patient for colonoscopy and to regulate and stabilize enterochromaffin cell secretory, pain and motility mechanisms, afferent fiber activity and GI and lower abdominal smooth muscle cells. The dosage is preferably oral and administration is preferably once or twice a day. The preferred first agent is tegaserod.

IC ICM A61K031-5513
ICS A61K031-445
INCL 514221000; 514282000; 514317000
CC 1-9 (Pharmacology)
Section cross-reference(s): 63
IT **Enkephalins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)
IT 5-HT reuptake inhibitors
Absorbents
Analgesics
Antacids
Anti-inflammatory agents
Antiemetics
Antiulcer agents
Anxiolytics
Atropa belladonna
Drug delivery systems
Drug interactions
Dyspepsia
Gastrointestinal agents
Gastrointestinal motility
Human
Immunomodulators

Laxatives
Muscarinic antagonists
Nausea
Ulcer
Vomiting
(combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)

IT **Opioids**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(κ-; combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)

IT 50-48-6, Amitriptyline 50-70-4, Sorbitol, biological studies 51-34-3, Scopolamine. 51-55-8, Atropine, biological studies 68-88-2, Hydroxyzine 69-72-7D, Salicylic acid, derivs. 77-19-0, Dicyclomine 89-57-6, Mesalamine. 101-31-5, Hyoscyamine. 114-07-8D, Erythromycin A, derivs. **125-71-3**, Dextromethorphan 364-62-5, Metoclopramide 438-41-5, LIBRIUM 439-14-5, VALIUM 446-86-6, Azathioprine 599-79-1, Sulfasalazine 603-50-9, Bisacodyl 915-30-0, Diphenoxylate 1134-47-0, ()-Baclofen 1229-29-4, Sinequan 1305-62-0, Calcium hydroxide, biological studies 7429-90-5D, Aluminum, compds. 7439-95-4D, Magnesium, compds. 8050-81-5, Simethicone 11041-12-6, Cholestyramine 12794-10-4D, Benzodiazepine, derivs. 14611-51-9, Selegiline 14882-18-9, Bismuth subsalicylate 15722-48-2, Olsalazine 28981-97-7, XANAX 34580-13-7, Ketotifen. 34911-55-2, Bupropion 37300-21-3, Pentosan polysulfate 51481-61-9, Cimetidine **53179-11-6**, Loperamide 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 57717-80-3, CGP7930 57808-66-9, Domperidone. 59729-33-8, Citalopram 60118-07-2D, Endorphin, analogs 61869-08-7, Paroxetine 66357-35-5, Ranitidine. 66514-99-6, S-Baclofen 69308-37-8, R-Baclofen 73590-58-6, Omeprazole 76824-35-6, Famotidine 76963-41-2, Nizatidine 79617-96-2, Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 83863-69-8, Nor-cisapride 89565-68-4, Tropisetron 90182-92-6, Zacopride 90667-30-4, Cyanodothiepin 92623-85-3, Milnacipran 93413-69-5, Venlafaxine 97964-56-2, Lorglumide 99614-02-5, Ondansetron 102625-70-7, Pantoprazole **103420-77-5**, L364718 103577-45-3, Lansoprazole. 104987-11-3, Tacrolimus 107097-80-3, Loxiglumide 109889-09-0, Granisetron 112727-80-7, Renzapride 112885-41-3, Mosapride 112922-55-1, Cericlamine 115607-61-9, SKF 96067 116539-59-4, Duloxetine 117976-89-3, Rabeprazole 119141-88-7, Esomeprazole 119817-90-2, Dexloxiglumide 120635-74-7, Cilansetron 122852-42-0, Alosetron 123040-69-7, Azasetron 123258-98-0, DAU 6285 123618-00-8, Fedotozine. 125787-94-2, FK-224 127595-43-1, BIMU 1 127618-28-4, DAU 6215 127729-35-5, SK&F97541 128794-94-5, Mycophenolate mofetil 129299-90-7, FK 1052 129623-01-4, GR82334 130404-91-0, CI 988 132036-88-5, Ramosetron 132746-60-2, CP-96345 133099-04-4, Darifenacin 133345-68-3, CGP44532 133345-73-0, CGP47656 134296-40-5, BIMU 8 135911-02-3, RP-67580 135938-17-9, SB 203186 136982-36-0, CP-99994 137196-67-9, SDZ 205-557 138449-07-7, FK 888 138752-34-8 141196-99-8, SC 53116 142001-63-6, SR-48968 144177-30-0, WIN 51708 144453-77-0, , SKF 97574 144625-51-4, GR 113808 144625-67-2, GR 125487 145158-71-0, Tegaserod 145742-28-5, CP122721 147523-65-7, LY288513. 148700-85-0, L 733060 148702-58-3, SB 204070 148703-08-6, SB 207710 149250-10-2, S-16474 149719-06-2, RS 23597 150705-88-7, CGP-49823 150785-53-8 151898-33-8, SC 53606 152811-62-6, SB 207266 152923-56-3, Daclizumab 153438-49-4, RPR-100893 153966-48-4, ANQ-11125 154967-61-0, L740093 155418-05-6, SR-140333 157351-81-0, MEN-10627 158364-59-1, BY 841 158848-32-9, GR-159897

158991-23-2, PD 154075 159706-39-5, L 742694 160472-97-9, , N 3389
161416-98-4, A-85380 166966-23-0, RPR-107880 167261-60-1, MDL-105212A
167710-87-4, RS 39604 167946-16-9 168266-90-8, GR 205171
168398-02-5, GR-203040 168570-35-2, PD-161182 168986-60-5, RS 67333
168986-61-6, RS 67506 169340-04-9, ZM-253270 170277-31-3, Infliximab
170566-84-4, LY 303870 170729-80-3, MK 869 171272-39-2, MEN-10930
171752-63-9, , ZD-7944 171859-02-2, RS 100235 172673-20-0, L758298
173050-51-6, SR-142801 174635-69-9, SB-222200 174636-32-9, SB-223412
174769-78-9, S18523 174858-27-6, OT 7100 175413-81-7, SB 205149
176390-32-2, LY0353433 178307-42-1, YH1885. 179045-86-4, Basiliximab
179474-81-8, Prucalopride 180046-99-5, SDZ-NKT-343 183005-37-0, SC
56184 187724-85-2, L 741671 188241-50-1, S19752 193694-35-8,
MDL-105172A 195889-55-5, YH1238 196004-82-7, SB 205800 196004-83-8,
SB 207058 201152-86-5, SR-144190 206052-25-7, MEN-11149 350610-61-6,
NKP-608A 439915-38-5, , L-743986 439915-38-5D, , L-743986, analogs
439915-42-1, RPR-106145 688320-93-6, R 59595 688321-02-0, DAU 6258
688321-03-1, H 40502 688321-07-5, BY 112 688321-08-6, L 363260
688321-17-7, ABT 269 688321-18-8, A 173508 688321-19-9, TKA 457
688321-21-3, RPR 111905 688321-22-4, YM 383336
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)

L29 ANSWER 71 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182525 HCAPLUS
DOCUMENT NUMBER: 140:210804
TITLE: Method of **analgesic** treatment with devazepide
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Ser. No. 349,431.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043990	A1	20040304	US 2003-410311	20030409
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		

PRIORITY APPLN. INFO.:
GB 2002-8129 A 20020409
US 2003-349431 A2 20030122
US 2002-53962 B2 20020122
US 2002-108659 A2 20020327

AB There is described a method of treatment of a patient requiring **analgesic** therapy which comprises the administration of an **analgesically** effective amount of devazepide. There is also described the use of devazepide in the manufacture of an **analgesically** effective medicament. Ten of seventeen patients had long-term pain relief (5-26 wk) with devazepide. The patients had pain with a neuropathic element and were taking regular, stable doses of strong opioids.
IC ICM A61K031-7052
ICS A61K031-5513; A61K031-485
INCL 514221000; 514023000; 514282000

CC 1-11 (Pharmacology)
ST devazepide **analgesic** neuropathic pain
IT **Analgesics**
Fillers
Human
Surfactants
(**analgesic** treatment with devazepide)
IT **Opioids**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. **analgesic**; **analgesic** treatment with devazepide)
IT Drug delivery systems
(bolus, injections; **analgesic** treatment with devazepide)
IT Drug delivery systems
(capsules; **analgesic** treatment with devazepide)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules; **analgesic** treatment with devazepide)
IT Drug delivery systems
(infusions; **analgesic** treatment with devazepide)
IT Drug delivery systems
(inhalants; **analgesic** treatment with devazepide)
IT Drug delivery systems
(injections, i.m.; **analgesic** treatment with devazepide)
IT Drug delivery systems
(injections, i.v.; **analgesic** treatment with devazepide)
IT Drug delivery systems
(injections, s.c.; **analgesic** treatment with devazepide)
IT Drug delivery systems
(intraarterial; **analgesic** treatment with devazepide)
IT Drug delivery systems
(intrathecal; **analgesic** treatment with devazepide)
IT Drug delivery systems
(nasal; **analgesic** treatment with devazepide)
IT Pain
(neuropathic; **analgesic** treatment with devazepide)
IT Nerve, disease
(neuropathy, pain; **analgesic** treatment with devazepide)
IT Drug delivery systems
(oral; **analgesic** treatment with devazepide)
IT Drug delivery systems
(rectal; **analgesic** treatment with devazepide)
IT Drug delivery systems
(transdermal; **analgesic** treatment with devazepide)
IT **103420-77-5**, Devazepide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesic** treatment with devazepide)
IT 52-26-6 **57-27-2**, Morphine, biological studies **57-27-2D**, Morphine, salts **57-42-1**, Meperidine **64-31-3**, Morphine sulfate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 561-27-3, Diamorphine 915-30-0, Diphenoxylate 20290-10-2,

Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**
, Tramadol **42408-82-2**, Butorphanol **52485-79-7**,
Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil
132875-61-7, Remifentanil
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. **analgesic**; **analgesic** treatment with
devazepide)

L29 ANSWER 72 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:836862 HCAPLUS
DOCUMENT NUMBER: 139:302070
TITLE: The use of devazepide as **analgesic** agent
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): Ml Laboratories PLC, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086409	A1	20031023	WO 2003-GB1514	20030409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481272	AA	20031023	CA 2003-2481272	20030409
EP 1492540	A1	20050105	EP 2003-725318	20030409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009139	A	20050201	BR 2003-9139	20030409
PRIORITY APPLN. INFO.:			GB 2002-8129 A	20020409
			WO 2003-GB1514 W	20030409

AB There is described a method of treatment of a patient requiring **analgesic** therapy which comprises the administration of an **analgesically** effective amount of devazepide. There is also described the use of devazepide in the manufacture of an **analgesically** effective medicament.
IC ICM A61K031-5513
ICS A61P025-04; A61P043-00
CC 1-11 (Pharmacology)
ST devazepide **analgesic** neuropathic pain opioid
IT Pain
Skin, disease
(allodynia; treatment of neuropathic pain with devazepide and in combination with opioid **analgesics**)
IT **Analgesics**
Human
(treatment of neuropathic pain with devazepide and in combination with opioid **analgesics**)

IT **Opioids**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neuropathic pain with devazepide and in combination with opioid **analgesics**)
IT 52-26-6, Morphine hydrochloride **57-27-2**, Morphine, biological studies **57-42-1**, Meperidine **64-31-3**, Morphine sulfate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 561-27-3, Heroin 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanyl **103420-77-5**, Devazepide 124417-48-7D, Hydroxymorphinan, derivs. **132875-61-7**, Remifentanyl
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neuropathic pain with devazepide and in combination with opioid **analgesics**)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 73 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777598 HCAPLUS
DOCUMENT NUMBER: 139:286355
TITLE: Use of devazepide for the treatment of constipation
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): ML Laboratories PLC, UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080066	A1	20031002	WO 2003-GB1285	20030326

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-7091 A 20020326
AB There is described a method of treatment of a patient suffering from constipation characterized in that the method comprises the administration of an effective amount of devazepide. There is also described a method of treatment of a patient requiring **analgesia** which comprises the sep., simultaneous or sequential administration of a therapeutically

effective amount of an **analgesic** and a laxative and/or stool softening amount of devazepide. The use of devazepide in the manufacture of a medicament is also described.

IC ICM A61K031-5513
ICS A61K031-485; A61P001-10

CC 1-9 (Pharmacology)
Section cross-reference(s): 63

ST devazepide laxative opioid **analgesic** constipation human

IT **Analgesics**
Human
Laxatives
(devazepide for treatment of constipation)

IT **Opioids**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide for treatment of constipation)

IT 52-26-6, Morphine hydrochloride **57-27-2**, Morphine, biological studies **57-42-1**, Meperidine **64-31-3**, Morphine sulfate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 561-27-3, Diamorphine 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil **132875-61-7**, Remifentanil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide for treatment of constipation)

IT 465-65-6, Naloxone **103420-77-5**, Devazepide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide for treatment of constipation)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 74 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:590987 HCAPLUS
DOCUMENT NUMBER: 139:138761
TITLE: Method of treatment of patients requiring **analgesia** with opioid **analgesics**
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): Ml Laboratories Plc, UK
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061632	A1	20030731	WO 2003-GB221	20030122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2473884	AA	20030731	CA 2003-2473884		20030122
EP 1467718	A1	20041020	EP 2003-708305		20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003007022	A	20041103	BR 2003-7022		20030122
JP 2005521655	T2	20050721	JP 2003-561577		20030122
PRIORITY APPLN. INFO.:			GB 2002-1367	A	20020122
			WO 2003-GB221	W	20030122

AB There is described a method of treatment of a patient requiring **analgesia** which comprises the sep., simultaneous or sequential administration of a therapeutically effective amount of an opioid **analgesic**, devazepide, and a surfactant. There is also described a monophasic pharmaceutical composition comprising devazepide effective in the enhancement of opioid **analgesia** and a surfactant. The daily dosage of devazepide is up to 0.7 mg/kg/day.

IC ICM A61K009-48
ICS A61K031-5513; A61K047-18; A61K047-20; A61P025-04; A61K031-485; A61K031-4468

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST opioid **analgesic analgesia**

IT Glycosides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(animal; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Drug delivery systems
(capsules; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters or ethers; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters with fatty acids; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Glycerides, biological studies
Sterols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Amides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fatty; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Lecithins
Lysophosphatidylcholines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Surfactants
(hydrophilic; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Surfactants
(hydrophobic; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(inhalants; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(injections, i.m.; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(injections, i.v.; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(injections, s.c.; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Surfactants
(ionic; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(liqs.; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT **Analgesia**
Antibacterial agents
Antimicrobial agents
Fillers
Human
Laxatives
Surfactants
(method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Bile acids
Bile salts
Diglycerides
Fatty acids, biological studies
Lecithins
Lysophosphatidylcholines
Lysophospholipids
Monoglycerides
Opioids
Peptides, biological studies
Phospholipids, biological studies
Sterols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT Drug delivery systems
(nasal; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Surfactants
(nonionic; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptides; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(oral; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(rectal; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(solids; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sugar esters; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(tablets; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Drug delivery systems
(transdermal; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, ethoxylated; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, hydrogenated; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable; method of treatment of patients requiring **analgesia** with opioid **analgesics**)
IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 52-26-6 **57-27-2**, Morphine, biological studies **57-42-1**, Meperidine 57-50-1, Sucrose, biological studies 57-55-6D, Propylene glycol, derivs. 63-42-3, Lactose **64-31-3**, Morphine sulfate 69-65-8, Mannitol 69-79-4D, Maltose, alkyl derivs. 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 77-92-9, Citric acid, biological studies **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 151-21-3, Sodium lauryl sulfate, biological studies 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 541-15-1D, Carnitine, analogs 557-04-0 561-27-3,

Diamorphine 577-11-7, Docusate sodium 915-30-0, Diphenoxylate 1119-97-7, Tetradecyltrimethylammonium bromide 5138-18-1D, Sulfosuccinic acid, alkyl esters 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7664-93-9D, Sulfuric acid, alkyl esters, salts 7757-93-9, Dibasic calcium phosphate 7778-18-9, Calcium sulfate 8044-71-1, Cetrimide 9005-25-8, Starch, biological studies 9005-25-8D, Starch, hydrolyzates 9005-32-7D, Alginic acid, salts 12441-09-7D, Sorbitan, esters with fatty acids 14807-96-6, Talc, biological studies 20290-10-2, Morphine-6-glucuronide 20408-97-3D, Thioglucose, alkyl derivs. **20594-83-6**, Nalbuphine 25322-68-3D, Polyethylene glycol, esters or ethers 25322-69-4D, Polypropylene glycol, esters with fatty acids **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil **103420-77-5**, Devacade 106392-12-5, Polyethylene glycol-polypropylene glycol block copolymer **132875-61-7**, Remifentanil 337376-15-5, Icodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method of treatment of patients requiring **analgesia** with opioid **analgesics**)

IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (microcryst.; method of treatment of patients requiring **analgesia** with opioid **analgesics**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L29 ANSWER 75 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:633285 HCAPLUS
DOCUMENT NUMBER: 139:159955
TITLE: Method and pharmaceutical composition using devazepide and surfactant with opioid **analgesic** therapy
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): ML Laboratories PLC, UK
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 108,659.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		
US 2004198723	A1	20041007	US 2002-53962	20020122
US 2003139396	A1	20030724	US 2002-108659	20020327
US 2004043990	A1	20040304	US 2003-410311	20030409
US 2004167146	A1	20040826	US 2003-622492	20030721
US 2004142959	A1	20040722	US 2004-752411	20040107

PRIORITY APPLN. INFO.:
US 2002-53962 B2 20020122
US 2002-108659 A2 20020327
GB 2002-1367 A 20020122
GB 2002-8129 A 20020409
US 2003-349431 A2 20030122

AB There is described a method of treatment of a patient requiring **analgesia** which comprises the sep., simultaneous or sequential administration of a therapeutically effective amount of an opioid

analgesic, devazepide and a surfactant. There is also described a monophasic pharmaceutical composition comprising an amount of devazepide effective in the enhancement of opioid **analgesia** and a pharmaceutically acceptable surfactant. The use of a surfactant is advantageous in that it improves the powder flow and/or separation properties of solid devazepide and also reduces or mitigates the undesirable side effects of opioid administration, e.g. constipation.

IC ICM A61K031-485
INCL 514282000
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
ST devazepide surfactant pharmaceutical enhancement opioid **analgesic** ; constipation opioid **analgesic** prevention surfactant
IT Amino acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-fatty acyl; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl ethers or alkylphenols; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Glycosides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl, alkylglucosides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Quaternary ammonium compounds, biological studies
Sulfates, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Glycosides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylthioglucosides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT **Opioids**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesics**; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(animal; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(bolus, injections; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(capsules; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Intestine, disease
(constipation, surfactant for reducing opioid-caused; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT **Analgesia**
Drug delivery systems
Fillers
Surfactants
(devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Alcohols, biological studies
Bile acids
Bile salts
Fatty acids, biological studies
Glycerides, biological studies
Lecithins
Lysophosphatidylcholines
Lysophospholipids
Phospholipids, biological studies
Sterols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Tocopherols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, with polyethylene glycol succinates; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, with polyglycerol or with polyethylene glycol ether with glycerol or sorbitan; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Fatty acids, biological studies
Glycerides, biological studies
Sterols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty acid esters; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Lecithins
Lysophosphatidylcholines
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Surfactants
(hydrophilic; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Surfactants
(hydrophobic; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(infusions, i.v.; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(inhalants; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(injections, i.m.; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(injections, i.v.; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(injections, intraarterial; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(injections, s.c.; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(intrathecal; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Surfactants
(ionic; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Glycerides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lauryl macrogolglycerides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(liqs.; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Alcohols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lower, fatty acid esters; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems
(nasal; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Surfactants
(nonionic; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptides, reaction products with fatty acids or glycerides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT **Analgesics**
(opioid; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT Drug delivery systems

(oral; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Drug delivery systems
(particles, coated with surfactant; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Alcohols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, reaction products with fatty acids or glycerides or (hydrogenated) vegetable oils or sterols; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with fatty acids or glycerides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Sterols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with polyols; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Amino acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products, derivs. with glycerides; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Glycerides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products, with polyols or sucrose; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products, with polyols; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Drug delivery systems
(rectal; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Drug delivery systems
(solids; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Monoglycerides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(succinoylated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Carbohydrates, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(sugar esters; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Carbohydrates, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sugar ethers; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Feces
(surfactant as softener for; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Antibacterial agents
Antimicrobial agents
Laxatives
(surfactant as; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Human
(surfactant for reducing opioid-caused; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Drug delivery systems
(tablets; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Drug delivery systems
(transdermal, patches; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, ethoxylated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, hydrogenated, ethoxylated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, hydrogenated; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, reaction products, with polyols; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT Fats and Glyceridic oils, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable, transesterified; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 77-92-9, Citric acid, biological studies 557-04-0, Magnesium stearate 7447-40-7, Potassium chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7757-93-9, Dibasic calcium phosphate 7778-18-9, Calcium sulfate 9004-34-6D, Cellulose,

compds. 9005-25-8, Starch, biological studies 9005-25-8D, Starch, hydrolyzed 14807-96-6, Talc, biological studies 337376-15-5, Icodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as filler; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT 57-50-1D, Sucrose, reaction products with glycerides, compds.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as surfactant or filler; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT **103420-77-5**, Devazepide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT **103420-82-2**
RL: MSC (Miscellaneous)
(devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT 50-21-5D, Lactic acid, oligomers, acyl derivs., reaction products with glycerides 52-26-6 56-81-5D, Glycerol, fatty acid esters, polyethylene glycol ethers **57-27-2**, Morphine, biological studies **57-27-2D**, Morphine, salts **57-42-1**, Meperidine 57-55-6D, Propylene glycol, reaction products with diglycerides **64-31-3**, Morphine sulfate 69-79-4D, Maltose, alkylmaltosides 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-42-6D**, Oxycodone, salts **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 77-92-9D, Citric acid, reaction products with glycerides 87-69-4D, Tartaric acid, monoacetylated or diacetylated, esters with glycerides 110-15-6D, Succinic acid, reaction products with monoglycerides **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 151-21-3, Sodium dodecyl sulfate, biological studies 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl **437-38-7D**, Fentanyl, salts 465-65-6, Naloxone **466-99-9**, Hydromorphone **466-99-9D**, Hydromorphone, salts 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 541-15-1D, Carnitine, reaction products with fatty acids 561-27-3, Diamorphine 577-11-7, Docusate sodium 915-30-0, Diphenoxylate 1119-97-7, Tetradecyltrimethyl ammonium bromide 5138-18-1D, Sulfosuccinic acid, salts, alkyl derivs. 8044-71-1, Cetrimide 9005-32-7D, Alginic acid, salts 9005-37-2, Propylene glycol alginate 12441-09-7D, Sorbitan, fatty acid esters, ethoxylated 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine 25322-68-3D, alkyl ethers or alkylphenols 25322-68-3D, Polyethylene glycol, fatty acid esters 25618-55-7D, Polyglycerol, fatty acid esters **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil 106392-12-5 **132875-61-7**, Remifentanil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

IT 25322-69-4, Polypropylene glycol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty acid esters; devazepide and surfactant monophasic pharmaceutical

composition for enhancement of opioid **analgesic**)
IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst., as filler; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)
IT 468-10-0D, Morphinan, compds.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid **analgesics**; devazepide and surfactant monophasic pharmaceutical composition for enhancement of opioid **analgesic**)

L29 ANSWER 76 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:570641 HCAPLUS
DOCUMENT NUMBER: 139:111675
TITLE: Method for constipation treatment
INVENTOR(S): Gibson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 4 pp., Cont.-in-part of U.S. Ser. No. 53,962.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003139396	A1	20030724	US 2002-108659	20020327
US 2004198723	A1	20041007	US 2002-53962	20020122
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		
US 2004167146	A1	20040826	US 2003-622492	20030721
US 2004142959	A1	20040722	US 2004-752411	20040107
PRIORITY APPLN. INFO.:			US 2002-53962	A2 20020122
			GB 2002-1367	A 20020122
			US 2002-108659	A2 20020327
			GB 2002-8129	A 20020409
			US 2003-349431	A2 20030122

AB Method is disclosed for the treatment of a patient suffering from constipation. Method comprises the administration of a therapeutically effective amount of devazepide. There is also described a method of treatment of a patient requiring **analgesia** which comprises the sep., simultaneous or sequential administration of a therapeutically effective amount of an **analgesic** and a stool softening amount of devazepide. The use of devazepide in the manufacture of a medicament is also described.
IC ICM A61K031-5513
INCL 514221000
CC 1-9 (Pharmacology)
Section cross-reference(s): 63
ST devazepide stool softener interaction **analgesic** delivery human constipation; laxative devazepide opioid **analgesic** pharmaceutical compn human constipation
IT **Analgesia**
Drug interactions
Human
Laxatives
(method for constipation treatment)
IT **Opioids**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for constipation treatment)

IT **Analgesics**
(opioid; method for constipation treatment)

IT 52-26-6 **57-27-2**, Morphine, biological studies **57-42-1**, Meperidine **64-31-3**, Morphine sulfate 76-41-5, Oxymorphone **76-42-6**, Oxycodone **76-57-3**, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine **125-28-0**, Dihydrocodeine **125-29-1**, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine **437-38-7**, Fentanyl 465-65-6, Naloxone **466-99-9**, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene 561-27-3, Diamorphine 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine **27203-92-5**, Tramadol **42408-82-2**, Butorphanol **52485-79-7**, Buprenorphine 54340-58-8, Meptazinol **71195-58-9**, Alfentanil **103420-77-5**, Devazepide **103420-82-2** 124417-48-7D, Hydroxymorphinan, compds. **132875-61-7**, Remifentanil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for constipation treatment)

L29 ANSWER 77 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:265895 HCAPLUS
DOCUMENT NUMBER: 130:316627
TITLE: **Analgesic** composition containing a CCK antagonist and an opioid
INVENTOR(S): Iversen, Leslie Lars
PATENT ASSIGNEE(S): Panos Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9918967	A1	19990422	WO 1998-GB3076		19981012
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9895475	A1	19990503	AU 1998-95475		19981012
EP 1023072	A1	20000802	EP 1998-949092		19981012
EP 1023072	B1	20021211			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001519396	T2	20011023	JP 2000-515602		19981012
AT 229337	E	20021215	AT 1998-949092		19981012
ES 2189252	T3	20030701	ES 1998-949092		19981012
PRIORITY APPLN. INFO.:			GB 1997-21746	A	19971015
			WO 1998-GB3076	W	19981012

AB Pharmaceutical formulations, particularly suitable for treating chronic and neuropathic pain comprise an opioid-potentiating amount of a cholecystokinin (CCK) antagonist and an **analgesic** amount of an opioid in a pharmaceutically acceptable biphasic carrier comprising an organic phase comprising a glyceride derivative and a hydrophilic phase. An i.v. emulsion contained L-740093 0.00025, morphine sulfate 0.10, phosphatidylcholine 0.024, Pluronic F68 0.0040 g, soy bean oil 0.4000 mL, and water q.s. 2 mL.

IC ICM A61K031-55
ICS A61K009-107; A61K009-20; A61K031-55; A61K031-485

CC 63-6 (Pharmaceuticals)

ST **analgesic** pharmaceutical cholecystokinin antagonist opioid; intravenous pharmaceutical emulsion L740093 morphine

IT **Analgesics**
(**analgesic** composition containing CCK antagonist and opioid)

IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesic** composition containing CCK antagonist and opioid)

IT Cottonseed oil
Gelatins, biological studies
Glycerides, biological studies
Olive oil
Peanut oil
Polymers, biological studies
Rape oil
Safflower oil
Soybean oil
Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesic** composition containing CCK antagonist and opioid)

IT Cholecystokinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **analgesic** composition containing CCK antagonist and opioid)

IT Drug delivery systems
(capsules, sustained-release; **analgesic** composition containing CCK antagonist and opioid)

IT Drug delivery systems
(emulsions, i.v.; **analgesic** composition containing CCK antagonist and opioid)

IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fish; **analgesic** composition containing CCK antagonist and opioid)

IT Diglycerides
Glycerides, biological studies
Monoglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated coco monoglycerides, diglycerides and triglycerides, Witepsol H 15, Witepsol W 25; **analgesic** composition containing CCK antagonist and opioid)

IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sesame; **analgesic** composition containing CCK antagonist and opioid)

IT Drug delivery systems
(suppositories; **analgesic** composition containing CCK antagonist and opioid)

IT Drug delivery systems
(tablets, sustained-release; **analgesic** composition containing CCK antagonist and opioid)
IT **64-31-3**, Morphine sulfate 125-72-4, Levorphanol tartrate
990-73-8, Fentanyl citrate 5965-13-9 58786-99-5, Butorphanol tartrate
103420-77-5, Mk 329 118101-09-0, l 365260 154967-61-0,
L-740093 170284-94-3, L 741528
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesic** composition containing CCK antagonist and opioid)
IT **57-27-2**, Morphine, biological studies **76-57-3**, Codeine
9003-39-8, Pvp 9004-32-4, Carboxymethyl cellulose 9004-61-9,
Hyaluronic acid 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5,
Methyl cellulose 9005-32-7, Alginic acid 9005-38-3, Sodium alginate
9032-42-2, Hydroxyethyl methyl cellulose 106392-12-5, Pluronic f68
109321-13-3, Suppocire dm 145878-26-8 223432-40-4 223435-96-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**analgesic** composition containing CCK antagonist and opioid)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 78 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:846822 HCAPLUS
DOCUMENT NUMBER: 123:219285
TITLE: Screening for gastrin-cholecystokinin type C receptor antagonists
INVENTOR(S): Baldwin, Graham Sherard
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9521380	A1	19950810	WO 1995-US1375		19950202
W: AU, CA, CN, FI, JP, KR, NO, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9517405	A1	19950821	AU 1995-17405		19950202
PRIORITY APPLN. INFO.:			AU 1994-3650	A	19940202
			AU 1994-6638	A	19940705
			AU 1994-7779	A	19940831
			WO 1995-US1375	W	19950202

AB The invention provides a method of identifying a compound having the ability to block the low-affinity gastrin-cholecystokinin type C receptor, comprising the step of measuring the ability of said compound to block the binding to gastrin-binding protein of a compound selected from the group consisting of a gastrin-related peptide, a cholecystokinin-related peptide, an antagonist of gastrin or of cholecystokinin, an acyl CoA, an enoyl CoA, an antibody to gastrin, and an antibody to cholecystokinin. Several ways in which the method of the invention can be carried out are described. Thus, the invention provides a general screening method for identifying antagonists of the gastrin-binding protein interaction, which are useful for treatment of diseases involving rapidly proliferating cells, and for controlling gastric acid secretion. Compns. and methods of treatment are also claimed.

IC ICM G01N033-53
ICS G01N033-573; A61K031-70; A61K038-16; A61K048-00
CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 1
IT 992-67-6, Crotonyl CoA 1420-36-6, Acetoacetyl CoA 1947-37-1, Tetragastrin 5534-95-2, Pentagastrin 6620-60-6, Proglumide 25126-32-3, Cholecystokinin-8 (pig) 25679-24-7, Nonsulfated cholecystokinin octapeptide 39544-74-6, Benzotript 60748-06-3, Gastrin-17 **103420-77-5**, L 364718 118101-09-0, L 365260
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(gastrin-cholecystokinin type C receptor antagonist screening by inhibition of gastrin-binding protein with gastrin analog)
IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 53-86-1, Indomethacin 61-68-7, Mefenamic acid 69-72-7, Salicylic acid, biological studies 103-90-2, Acetaminophen 644-62-2 4394-00-7, Niflumic acid **15307-86-5**, Diclofenac 15687-27-1, Ibuprofen 22204-53-1, Naproxen **22494-42-4**, Diflunisal 26171-23-3, Tolmetin 33005-95-7, Tiaprofenic acid 36322-90-4, Piroxicam 38194-50-2, Sulindac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrin-cholecystokinin type C receptor antagonist screening by inhibition of gastrin-binding protein with gastrin analog)

L29 ANSWER 79 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:617859 HCAPLUS
DOCUMENT NUMBER: 119:217859
TITLE: Enhancement of opiate **analgesia** by devazepide in a baboon dolorimetry model
AUTHOR(S): Klein, Hilton; Jackson, Robert; McCormick, Gwendolyn; Montgomery, Tamara; Frankenfield, Dale; Pouch, Walter; Soper, Keith; Murray, Kathy
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Mult. Cholecystokinin Recept. CNS (1992), 529-36. Editor(s): Dourish, Colin T. Oxford Univ. Press: Oxford, UK.
CODEN: 59HNAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Dental dolorimetry in the baboon showed that the CCK antagonist derazepide potentiated alfentanil **analgesia** by an interaction that does not involved neural pathways other than those related to pain.
CC 2-6 (Mammalian Hormones)
ST opiate **analgesia** CCK antagonist devazepide
IT **Opioids**
RL: BIOL (Biological study)
(**analgesia** from, devazepide enhancement of, in baboon)
IT **Analgesia**
(from opiates, devazepide enhancement of, in baboon)
IT 9011-97-6, Cholecystokinin
RL: BIOL (Biological study)
(blockade of, opiate **analgesia** enhancement by, in baboon)
IT **103420-77-5**, Devazepide
RL: BIOL (Biological study)
(opiate **analgesia** enhancement by, in baboon)

L29 ANSWER 80 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:559189 HCAPLUS

DOCUMENT NUMBER: 115:159189
TITLE: Preparation of benzodiazepine analogs for treating panic syndrome and for directly inducing **analgesia**
INVENTOR(S): Bock, Mark G.; Freidinger, Roger M.; Dourish, Colin T.; Iversen, Susan; Evans, Ben E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 434364	A2	19910626	EP 1990-313847	19901218
EP 434364	A3	19920401		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2032222	AA	19910619	CA 1990-2032222	19901213
AU 9068151	A1	19910620	AU 1990-68151	19901217
ZA 9010124	A	19910925	ZA 1990-10124	19901217
JP 06009580	A2	19940118	JP 1990-419340	19901218
PRIORITY APPLN. INFO.:			US 1989-452023 A	19891218

OTHER SOURCE(S): MARPAT 115:159189
AB Title compds. [I; R1 = H, alkyl, cycloalkylalkyl, aminoalkyl, alkoxyalkyl, carbamoylalkyl, etc.; R2 = (substituted) Ph, pyridyl, alkoxycarbonylalkyl, etc.; R3 = NHCOR5, NHCONHR5, COR5, NHCOCH2R5; R4 = H, NO2, CF3, alkyl, halo; R5 = naphthyl, (substituted) Ph, pyridyl, indolyl, styryl, 2-aminopyridyl, etc.; R6 = H, OH; r = 1,2], were prepared Thus, 3S-3-amino-1,3-dihydro-3-(2-indolecarbonylamino)-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one in CH2Cl2 was treated with 2-indolecarbonyl chloride and Et3N and the mixture was stirred 30 min to give title compound 3S-II. The latter at 0.05-5.0 μg/kg s.c. in mice was an effective anxiolytic in the black/white exploration test of Crawley, and at 0.1 mg/kg s.c. in rats increased exploratory activity in novel environments.
IC ICM A61K031-55
CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT **Analgesics**
Anesthetics
(benzodiazepinones)
IT 103342-81-0P 103342-82-1P 103343-53-9P 103343-55-1P 103343-59-5P
103373-45-1P 103407-25-6P **103420-77-5P** 103420-78-6P
103420-81-1P 111035-59-7P 116842-93-4P 116842-99-0P 118018-40-9P
118101-08-9P 118101-09-0P 119486-85-0P 119486-87-2P 119486-88-3P
119486-90-7P 119486-92-9P 119486-93-0P 119486-95-2P 119487-00-2P
119487-10-4P 119487-14-8P 119566-30-2P 128066-71-7P 136051-05-3P
136051-07-5P 136051-11-1P 136051-13-3P 136162-58-8P 136162-59-9P
136162-62-4P 136162-63-5P 136162-64-6P 136162-65-7P 136162-69-1P
136162-71-5P 136162-72-6P 136162-73-7P 136162-74-8P 136234-81-6P
136234-82-7P 136234-83-8P 170228-74-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholecystokinin and gastrin antagonist for treatment of panic disorder)

L29 ANSWER 81 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:417799 HCAPLUS
DOCUMENT NUMBER: 113:17799

TITLE: Cholecystokinin antagonists proglumide, lorglumide and benzotript, but not L-364,718, interact with brain opioid binding sites
AUTHOR(S): Gaudreau, P.; Lavigne, G. J.; Quirion, R.
CORPORATE SOURCE: Res. Cent., Notre-Dame Hosp., Montreal, QC, H2L 4MI, Can.
SOURCE: Neuropeptides (Edinburgh, United Kingdom) (1990), 16(1), 51-5
CODEN: NRPPDD; ISSN: 0143-4179
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been reported that proglumide and L-367,718 potentiate opioid-induced antinociception. However, their mode of action in pain modulation is still not understood. To evaluate a possible interaction with opioid receptors, the affinities of the cholecystokinin (CCK) antagonists proglumide, lorglumide, benzotript, and L-367,718 on μ, δ, and κ binding sites were determined, using guinea pig brain crude synaptosome prepns. These affinities were compared to that of the central CCK binding site, using rat brain slide-mounted sections. At 100 μM, proglumide competed for 13 and 17% of μ and κ binding sites, but did not interact with δ and CCK sites. At this concentration, lorglumide reduced μ, δ, κ, and CCK specific binding by 44, 69, 35, and 88%, whereas benzotript diminished it by 16, 13, 38, and 48%, resp. L-364,718 did not interact with opioid receptors (assay limit of solubility, 10 μM) but had a high affinity for CCK binding sites (IC50, 126 nM). The lack of selectivity of proglumide, lorglumide, and benzotript for CCK receptors suggests that their reported ability to potentiate morphine **analgesia** may be related to an interaction with opioid receptors.

CC 1-11 (Pharmacology)

IT 6620-60-6, Proglumide 39544-74-6, Benzotript 97964-56-2, Lorglumide **103420-77-5**, L-364718
RL: BIOL (Biological study)
(opioid receptors of brain binding response to)

L29 ANSWER 82 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:417446 HCAPLUS
DOCUMENT NUMBER: 113:17446
TITLE: Effects of protein binding and experimental disease states on brain uptake of benzodiazepines in rats
AUTHOR(S): Lin, Tsu Han; Lin, Jiunn H.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1990), 253(1), 45-50
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The brain uptake of 4 benzodiazepines with different lipophilic and protein binding characteristics was investigated in male rats following rapid intracarotid artery injection. When the compds. were administered as a solution in Ringer's buffer, pH 7.4, the uptake was in the order [14C]diazepam > [14C]L-663,581 (anxiolytic agent) > {3H]L-364,718 (morphine **analgesia** potentiator) > [14C]L-365,260 (anxiolytic agent), and their extraction ratios were 71.0, 65.0, 42.0, 6.0%, resp. The resp. permeability-surface product values were 0.755, 0.647, 0.329, and 0.035 mL/min/g. The rank order of brain extraction did not correlate well with the drugs' lipophilicity as determined by the octanol-buffer partition coefficient

devazepide: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
n allylnormetazocine: PD, pharmacology
morphine sulfate: PD, pharmacology
dynorphin[1-8]: PD, pharmacology
cholecystokinin octapeptide: PD, pharmacology
gastrin: PD, pharmacology
unindexed drug
unclassified drug

RN (metenkephalin) 58569-55-4; (leucine enkephalin) 58822-25-6; (beta funaltrexamine) 72782-05-9; (enkephalin[2 dextro alanine 5 dextro leucine]) 63631-40-3; (ethylketazocine) 36292-66-7; (naloxone) 357-08-4, 465-65-6; (metenkephalin[6 arginine 7 phenylalanine]) 73024-95-0; (proenkephalin) 90880-95-8; (beta endorphin) 59887-17-1; (alpha neoendorphin) 69671-17-6; (dynorphin B) 85006-82-2; (levacetylmethadol) 34433-66-4; (somatostatin) 38916-34-6, 51110-01-1; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (enkephalin[2,5 dextro penicillamine]) 88373-73-3, 88381-29-7; (n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide) 96744-75-1; (devazepide) **103420-77-5**; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (n allylnormetazocine) 14198-28-8; (morphine sulfate) 23095-84-3, 35764-55-7, 64-31-3; (dynorphin[1-8]) 75790-53-3; (cholecystokinin octapeptide) 25126-32-3; (gastrin) 9002-76-0

CN U 69593; L 364718; L 365260; Skf 10047

GEN GENBANK AF156878 referred number; GENBANK AF172449 referred number; GENBANK AF172450 referred number; GENBANK AF172451 referred number; GENBANK AF172452 referred number; GENBANK AF172453 referred number

L29 ANSWER 86 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002054728 EMBASE
TITLE: Review article: Transient lower oesophageal sphincter relaxations - A pharmacological target for gastro-oesophageal reflux disease?.
AUTHOR: Hirsch D.P.; Tytgat G.N.J.; Boeckxstaens G.E.E.
CORPORATE SOURCE: Dr. G.E.E. Boeckxstaens, Academic Medical Centre, Division of Gastroenterology, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands. g.e.boeckxstaens@amc.uva.nl
SOURCE: Alimentary Pharmacology and Therapeutics, (2002) Vol. 16, No. 1, pp. 17-26.
Refs: 98
ISSN: 0269-2813 CODEN: APTHEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020221
Last Updated on STN: 20020221

AB The oesophago-gastric junction functions as an anti-reflux barrier preventing increased exposure of the oesophageal mucosa to gastric contents. Failure of this anti-reflux barrier results in gastro-oesophageal reflux disease, and may lead to complications such as oesophagitis, Barrett's oesophagus and eventually oesophageal carcinoma. Recent studies have suggested that transient lower oesophageal sphincter

relaxation is the main mechanism underlying gastro-oesophageal reflux. It involves a prolonged relaxation of the lower oesophageal sphincter, mediated by a vago-vagal neural pathway, synapsing in the brainstem. Several drugs, such as atropine, baclofen and loxiglumide, have been shown to reduce the rate of transient lower oesophageal sphincter relaxations and concomitantly the number of reflux episodes. These findings illustrate that transient lower oesophageal sphincter relaxations may represent a potential new target for the pharmacological treatment of gastro-oesophageal reflux disease. It is possible that the reduction in the number of transient lower oesophageal sphincter relaxations may also contribute to the beneficial effect of fundoplication and new endoscopic anti-reflux procedures. It should be emphasized, however, that other factors, such as low lower oesophageal sphincter pressure, the presence of a hiatal hernia and impaired oesophageal peristalsis, are also of great importance. Therefore. whether the targeting of transient lower oesophageal sphincter relaxations is the 'golden bullet' in anti-reflux therapy remains to be proven, as evidence of an effective control of gastro-oesophageal reflux in reflux patients is still lacking.

CT Medical Descriptors:
*lower esophagus sphincter
*gastroesophageal reflux: DT, drug therapy
*gastroesophageal reflux: SU, surgery
esophagitis: CO, complication
Barrett esophagus: CO, complication
esophagus carcinoma: CO, complication
stomach fundoplication
hiatus hernia
esophagus motility
human
review
priority journal
Drug Descriptors:
atropine: CM, drug comparison
atropine: DT, drug therapy
atropine: PD, pharmacology
baclofen: CM, drug comparison
baclofen: DT, drug therapy
baclofen: PD, pharmacology
loxiglumide: CB, drug combination
loxiglumide: CM, drug comparison
loxiglumide: DT, drug therapy
loxiglumide: PD, pharmacology
morphine: CM, drug comparison
morphine: DT, drug therapy
morphine: PD, pharmacology
riluzole: CM, drug comparison
riluzole: DT, drug therapy
riluzole: PD, pharmacology
nitric oxide synthase inhibitor: CM, drug comparison
nitric oxide synthase inhibitor: DT, drug therapy
nitric oxide synthase inhibitor: PD, pharmacology
devazepide: CB, drug combination
devazepide: CM, drug comparison
devazepide: DT, drug therapy
devazepide: PD, pharmacology

RN (atropine) 51-55-8, 55-48-1; (baclofen) 1134-47-0; (loxiglumide) 107097-80-3; (morphine) 52-26-6, 57-27-2; (riluzole) 1744-22-5; (devazepide) **103420-77-5**

L29 ANSWER 87 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002439670 EMBASE
TITLE: Novel medical therapies for gastroesophageal reflux disease beyond proton-pump inhibitors.
AUTHOR: Richter J.E.
CORPORATE SOURCE: Dr. J.E. Richter, Department of Gastroenterology, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States
SOURCE: Gastroenterology Clinics of North America, (2002) Vol. 31, No. 4 SUPPL., pp. S111-S116.
Refs: 14
ISSN: 0889-8553 CODEN: GCNAEF
PUBLISHER IDENT.: S 0889-8553(02)00045-6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20021227

AB The control of TLESRs is a novel pharmacologic approach to the treatment of GERD. It is applicable in most reflux patients characterized as having nonerosive disease or patients with mild erosive disease. Currently, only the GABAB agonist baclofen is available for oral therapy, although side effects may be a limiting factor. Future drug development requires a better understanding of the central and peripheral mechanisms controlling TLESRs.

CT Medical Descriptors:
*gastroesophageal reflux: DT, drug therapy
symptomatology
side effect: SI, side effect
smooth muscle relaxation
morphine addiction: SI, side effect
constipation: SI, side effect
drowsiness: SI, side effect
nausea: SI, side effect
seizure: SI, side effect
human
review
Drug Descriptors:
*proton pump inhibitor: DT, drug therapy
*4 aminobutyric acid B receptor stimulating agent: AE, adverse drug reaction
*4 aminobutyric acid B receptor stimulating agent: DT, drug therapy
*4 aminobutyric acid B receptor stimulating agent: PO, oral drug administration
*cholecystokinin receptor blocking agent: DT, drug therapy
*cholecystokinin receptor blocking agent: IV, intravenous drug administration
*cholinergic receptor blocking agent: AE, adverse drug reaction
*cholinergic receptor blocking agent: DT, drug therapy
*cholinergic receptor blocking agent: IV, intravenous drug administration
*nitric oxide synthase inhibitor: DT, drug therapy
***morphine: AE, adverse drug reaction**
***morphine: DT, drug therapy**
***morphine: IV, intravenous drug administration**

baclofen: AE, adverse drug reaction
baclofen: DT, drug therapy
baclofen: PO, oral drug administration
cholecystokinin A receptor antagonist: DT, drug therapy
cholecystokinin A receptor antagonist: IV, intravenous drug administration
cholecystokinin B receptor antagonist: DT, drug therapy
cholecystokinin B receptor antagonist: IV, intravenous drug administration
devazepide
loxiglumide: DT, drug therapy
loxiglumide: IV, intravenous drug administration
atropine: AE, adverse drug reaction
atropine: DT, drug therapy
atropine: IV, intravenous drug administration
nitric oxide
loperamide: AE, adverse drug reaction
loperamide: DT, drug therapy

RN (morphine) 52-26-6, 57-27-2; (baclofen) 1134-47-0; (devazepide) **103420-77-5**; (loxiglumide) 107097-80-3; (atropine) 51-55-8, 55-48-1; (nitric oxide) 10102-43-9; (loperamide) 34552-83-5, 53179-11-6

L29 ANSWER 88 OF 124 EMBASE on STN

ACCESSION NUMBER: 2001434496 EMBASE
TITLE: Evidence for ε-opioid receptor-mediated β-endorphin-induced analgesia.
AUTHOR: Tseng L.F.
CORPORATE SOURCE: L.F. Tseng, Dept. of Anesthesiology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States. Itseng@mcw.edu
SOURCE: Trends in Pharmacological Sciences, (1 Dec 2001) Vol. 22, No. 12, pp. 623-630.
Refs: 60
ISSN: 0165-6147 CODEN: TPHSDY
PUBLISHER IDENT.: S 0165-6147(00)01843-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020103
Last Updated on STN: 20020103

AB Among the opioid receptors, which have been pharmacologically classified as μ, δ, κ and ε, the existence of the ε receptor has been controversial, and this receptor is generally not recognized as a member of the opioid peptide receptor family because it has not been precisely characterized. However, results from pharmacological, physiological and opioid receptor binding studies clearly indicate the presence of ε-opioid receptors, which are distinct from μ-, δ- or κ-opioid receptors. This putative ε-opioid receptor is stimulated supraspinally by the endogenous opioid peptide β-endorphin, which induces the release of Met-enkephalin, which, in turn, acts on spinal δ2-opioid receptors to produce antinociception. In this article, this β-endorphin-sensitive ε-opioid receptor-mediated descending pain control system, which is distinct from that activated by the μ-opioid receptor agonist morphine, is described and the physiological role of the β-endorphin-mediated system in pain control activated by cold-water swimming and intraplantar injection of formalin is discussed.

CT Medical Descriptors:
*analgesia
receptor binding
pain
antinociception
swimming
cross tolerance
brain region
tail flick test
nerve tract
nociception
nonhuman
review
priority journal
Drug Descriptors:
*epsilon opiate receptor: EC, endogenous compound
*beta endorphin
mu opiate receptor: EC, endogenous compound
delta opiate receptor: EC, endogenous compound
kappa opiate receptor: EC, endogenous compound
metenkephalin: EC, endogenous compound
dextro phenylalanylcysteinyltyrosyl dextro tryptophylornithylthreonylpenic
illaminylthreoninamide 2,7 disulfide: PD, pharmacology
beta funaltrexamine: PD, pharmacology
naltrindole: PD, pharmacology
n,n diallyltyrosyl 2 methylalanyl 2 methylalanylphenylalanylleucine: PD,
pharmacology
binaltorphimine: PD, pharmacology
morphine
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]
3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide
methanesulfonate
quadazocine: PD, pharmacology
antisense oligodeoxynucleotide: PD, pharmacology
cytidine triphosphate: PD, pharmacology
naltrindole isothiocyanate: PD, pharmacology
delta opiate receptor antagonist: PD, pharmacology
cholecystokinin octapeptide: PD, pharmacology
pd 135158
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3
methylphenyl)urea: PD, pharmacology
4 aminobutyric acid: EC, endogenous compound
pentobarbital: PD, pharmacology
4 aminobutyric acid receptor: EC, endogenous compound
glutamate receptor: EC, endogenous compound
nitric oxide: EC, endogenous compound
cyclic GMP: EC, endogenous compound
pertussis toxin
unindexed drug
unclassified drug
devazepide
dizocilpine
2 bromo n (2 chloroethyl) n ethylbenzylamine
3 amino 2 (3 carboxypropyl) 6 (4 methoxyphenyl)pyridazinium bromide
1,2,3,4,4a,5,12,12aalpha octahydro 4aalpha (3 hydroxyphenyl) 2
methylquinolino[2,3 g]isoquinoline
RN (beta endorphin) 59887-17-1; (metenkephalin) 58569-55-4; (dextro
phenylalanylcysteinyltyrosyl dextro tryptophylornithylthreonylpenicillamin
ylthreoninamide 2,7 disulfide) 103429-31-8; (beta funaltrexamine)

72782-05-9; (naltrindole) 111555-53-4; (n,n diallyltyrosyl 2 methylalanyl 2 methylalanylphenylalanylleucine) 89352-67-0; (binaltorphimine) 105618-27-7; (morphine) 52-26-6, 57-27-2; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate) 83913-06-8; (quadazocine) 71276-43-2, 77844-05-4; (cytidine triphosphate) 65-47-4; (cholecystokinin octapeptide) 25126-32-3; (pd 135158) 130325-35-8; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 aminobutyric acid) 28805-76-7, 56-12-2; (pentobarbital) 57-33-0, 76-74-4; (nitric oxide) 10102-43-9; (cyclic GMP) 7665-99-8; (pertussis toxin) 70323-44-3; (devazepide) **103420-77-5** ; (dizocilpine) 77086-21-6; (2 bromo n (2 chloroethyl) n ethylbenzylamine) 40616-75-9; (3 amino 2 (3 carboxypropyl) 6 (4 methoxyphenyl)pyridazinium bromide) 104104-50-9; (1,2,3,4,4a,5,12,12aalpha octahydro 4aalpha (3 hydroxyphenyl) 2 methylquinolino[2,3 g]isoquinoline) 148545-09-9, 173398-79-3, 189263-70-5

CN Ici 174864; Win 44441; L 365260; L 364718; Mk 801; Dsp 4; Pd 135158; Sr 95531; Tan 67; U 50488h

L29 ANSWER 89 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002013874 EMBASE
TITLE: Systemic pharmacomodulation of transient lower esophageal sphincter relaxations.
AUTHOR: Holloway R.H.
CORPORATE SOURCE: Dr. R.H. Holloway, Department of Gastroenterology, Royal Adelaide Hospital, University of Adelaide, Adelaide, Australia
SOURCE: American Journal of Medicine, (3 Dec 2001) Vol. 111, No. 8 SUPPL. 1, pp. 178S-185S.
Refs: 61
ISSN: 0002-9343 CODEN: AJMEAZ
PUBLISHER IDENT.: S 0002-9343(01)00853-1
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020117
Last Updated on STN: 20020117

AB Transient lower esophageal sphincter relaxations (TLESRs) are the major mechanism of reflux in patients with gastroesophageal reflux disease. They are therefore attractive targets for pharmacotherapy. During the past 5 years, there has been a burgeoning interest in the neural pathways that control these events and in the pharmacologic receptors involved in these pathways. Several agents have been shown to reduce the rate of TLESRs, including cholecystokinin-A antagonists, anticholinergic agents, nitric oxide synthase inhibitors, morphine, somatostatin, serotonin type 3-receptor antagonists, and γ-aminobutyric acid-B (GABA(B)) agonists. Their predominant site of action appears to be on either the afferent pathways and/or the central integrative mechanisms within the dorsal vagal complex in the brainstem. Most of the agents tested are unsuitable for clinical use either because of side effects or because of the lack of an orally effective formulation. The most promising agents identified to date are the GABA(B) agonists. Baclofen, the prototype

GABA(B) agonist, inhibits the rate of TLESRs by more than 50%. Control of TLESRs is a major new approach to the treatment of reflux disease. It is likely to be applicable to the majority of patients, particularly those without macroscopic mucosal lesions or only mild erosive disease. Further development of more effective agents will depend both on a better understanding of the neural pathways and receptors involved in the control of TLESRs, as well as on investigation of other novel agents. At present, inhibition of TLESRs is at the threshold of transition from concept to practical use. Whether it makes the final leap into the mainstream of therapy will depend on the development of new, novel, and well-targeted pharmacologic agents. .COPYRGT. 2001 by Excerpta Medica, Inc.

CT Medical Descriptors:
*gastroesophageal reflux: DT, drug therapy
*gastroesophageal reflux: ET, etiology
*esophagus motility
side effect: SI, side effect
drug mechanism
drug effect
lower esophagus sphincter
sensory nerve
treatment outcome
drug efficacy
vagus nerve dorsal nucleus
brain stem
human
nonhuman
conference paper
priority journal
Drug Descriptors:
mu opiate receptor agonist: DT, drug therapy
mu opiate receptor agonist: PD, pharmacology
mu opiate receptor antagonist: DT, drug therapy
mu opiate receptor antagonist: PD, pharmacology
serotonin 3 antagonist: DT, drug therapy
serotonin 3 antagonist: PD, pharmacology
cholecystokinin receptor stimulating agent: DT, drug therapy
cholecystokinin receptor stimulating agent: PD, pharmacology
4 phosphonomethylpipecolic acid: DT, drug therapy
4 phosphonomethylpipecolic acid: PD, pharmacology
naloxone: DT, drug therapy
naloxone: PD, pharmacology
ondansetron: DT, drug therapy
ondansetron: PD, pharmacology
granisetron: DT, drug therapy
granisetron: PD, pharmacology
cholecystokinin A receptor antagonist: DT, drug therapy
cholecystokinin A receptor antagonist: PD, pharmacology
n(g) nitroarginine methyl ester: DT, drug therapy
n(g) nitroarginine methyl ester: PD, pharmacology
nitric oxide synthase inhibitor: DT, drug therapy
nitric oxide synthase inhibitor: PD, pharmacology
n(g) methylarginine: DT, drug therapy
n(g) methylarginine: PD, pharmacology
morphine: DT, drug therapy
morphine: PD, pharmacology
morphine: IV, intravenous drug administration
somatostatin: DT, drug therapy
somatostatin: PD, pharmacology
4 aminobutyric acid B receptor stimulating agent: AE, adverse drug

reaction
4 aminobutyric acid B receptor stimulating agent: DT, drug therapy
4 aminobutyric acid B receptor stimulating agent: PD, pharmacology
scopolamine butyl bromide: DT, drug therapy
scopolamine butyl bromide: PD, pharmacology
methylscopolamine: DT, drug therapy
methylscopolamine: PD, pharmacology
atropine: DT, drug therapy
atropine: PD, pharmacology
baclofen: DT, drug therapy
baclofen: PD, pharmacology
cholecystokinin octapeptide: DT, drug therapy
cholecystokinin octapeptide: PD, pharmacology
arginine: DT, drug therapy
arginine: PD, pharmacology
devazepide: AD, drug administration
devazepide: DT, drug therapy
devazepide: PD, pharmacology
devazepide: CV, intracerebroventricular drug administration
loxiglumide: DT, drug therapy
loxiglumide: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
4 aminobutyric acid B receptor blocking agent: DT, drug therapy
4 aminobutyric acid B receptor blocking agent: PD, pharmacology
4 aminobutyric acid B receptor blocking agent: PO, oral drug administration
dicycloverine: DT, drug therapy
dicycloverine: PD, pharmacology
cholinergic receptor blocking agent: DT, drug therapy
cholinergic receptor blocking agent: PD, pharmacology
muscarinic receptor blocking agent: DT, drug therapy
muscarinic receptor blocking agent: PD, pharmacology
unindexed drug

RN (4 phosphonomethylpipecolic acid) 110347-85-8; (naloxone) 357-08-4, 465-65-6; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (granisetron) 107007-99-8, 109889-09-0; (n(g) nitroarginine methyl ester) 50903-99-6; (n(g) methylarginine) 156706-47-7, 17035-90-4; (morphine) 52-26-6, 57-27-2; (somatostatin) 38916-34-6, 51110-01-1; (scopolamine butyl bromide) 149-64-4, 7182-53-8, 73156-19-1; (methylscopolamine) 13265-10-6; (atropine) 51-55-8, 55-48-1; (baclofen) 1134-47-0; (cholecystokinin octapeptide) 25126-32-3; (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (devazepide) **103420-77-5**; (loxiglumide) 107097-80-3; (dicycloverine) 50815-09-3, 67-92-5, 77-19-0

CN Cgs 19755

L29 ANSWER 90 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000007781 EMBASE
TITLE: Therapeutic and chemical developments of cholecystokinin receptor ligands.
AUTHOR: De Tullio P.; Delarge J.; Pirotte B.
CORPORATE SOURCE: P. De Tullio, Department of Medicinal Chemistry, Universite de Liege, C.H.U., Avenue de l'Hopital 1, B-4000 Sart-Tilman (Liege), Belgium. P.Detullio@ulg.ac.be
SOURCE: Expert Opinion on Investigational Drugs, (2000) Vol. 9, No. 1, pp. 129-146.
Refs: 111
ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113

AB Cholecystokinin (CCK) is an important 'brain-gut' hormone located both in the gastrointestinal (GI) system and in the CNS. At least two different G-coupled high affinity receptors have been identified: the CCK-A and the CCK-B receptors. Although the complex biological role of CCK is, as yet, not fully understood, its connection with many different physiological processes both at the GI level and at the CNS level is now well established. There is much potential for therapeutic use of CCK receptor ligands, however, clear investigations have yet to be completed. Several chemical families have been investigated over the last 20 years to find potent, subtype selective and stable CCK receptor agonists and antagonists. The main goal was to discover new therapeutic drugs acting on GI and/or on CNS diseases and also, to obtain powerful pharmacological tools that could permit a better understanding of the biological role of CCK. Despite promising results from investigations into medicinal chemistry of CCK receptor ligands, the therapeutical applications of these ligands still remains to be defined. This article reviews the main biological role of CCK, the therapeutic potential of CCK-A and CCK-B receptor agonists and antagonists and the common compounds from the different families of ligands.

CT Medical Descriptors:
drug synthesis
drug potency
drug selectivity
central nervous system disease
gastrointestinal disease
drug antagonism
pancreatitis
irritable colon
human
nonhuman
review
Drug Descriptors:
*cholecystokinin receptor stimulating agent: DV, drug development
*cholecystokinin receptor blocking agent: DV, drug development
G protein coupled receptor: EC, endogenous compound
cholecystokinin receptor: EC, endogenous compound
receptor subtype: EC, endogenous compound
cholecystokinin A receptor: EC, endogenous compound
cholecystokinin B receptor: EC, endogenous compound
morphine: PD, pharmacology
cholecystokinin: EC, endogenous compound
cholecystokinin: PD, pharmacology
beta endorphin: PD, pharmacology
benzotript: DV, drug development
benzotript: PD, pharmacology
proglumide: DV, drug development
proglumide: PD, pharmacology
lorglumide: DV, drug development
lorglumide: PD, pharmacology
loxiglumide: DV, drug development
loxiglumide: PD, pharmacology

cam 1481: DV, drug development
cam 1481: PD, pharmacology
devazepide: DV, drug development
devazepide: PD, pharmacology
n [1 (2 fluorophenyl) 3,4,6,7 tetrahydro 4 oxopyrrolo[3,2,1 jk][1,4]benzodiazepin 3 yl] 1h indole 2 carboxamide: DV, drug development
n [1 (2 fluorophenyl) 3,4,6,7 tetrahydro 4 oxopyrrolo[3,2,1 jk][1,4]benzodiazepin 3 yl] 1h indole 2 carboxamide: PD, pharmacology
ly 219057: DV, drug development
ly 219057: PD, pharmacology
sc 50998: DV, drug development
sc 50998: PD, pharmacology
iqm 95333: DV, drug development
iqm 95333: PD, pharmacology
tp 680: DV, drug development
tp 680: PD, pharmacology
t 0632: DV, drug development
t 0632: PD, pharmacology
ceruletide: DV, drug development
ceruletide: PD, pharmacology
a 71378: DV, drug development
a 71378: PD, pharmacology
n tert butyloxycarbonyltryptophyl[nepsilon (2 methylphenylaminocarbonyl)lysyl]aspartyl n methylphenylalaninamide: DV, drug development
n tert butyloxycarbonyltryptophyl[nepsilon (2 methylphenylaminocarbonyl)lysyl]aspartyl n methylphenylalaninamide: PD, pharmacology
ar r15849: DV, drug development
ar r15849: PD, pharmacology
gw 7178: DV, drug development
gw 7178: PD, pharmacology
gw 5823: DV, drug development
gw 5823: PD, pharmacology
unindexed drug

RN (morphine) 52-26-6, 57-27-2; (cholecystokinin) 9011-97-6, 93443-27-7; (beta endorphin) 59887-17-1; (benzotript) 39544-74-6; (proglumide) 6620-60-6; (lorglumide) 97964-56-2; (loxiglumide) 107097-80-3; (devazepide) **103420-77-5**; (n [1 (2 fluorophenyl) 3,4,6,7 tetrahydro 4 oxopyrrolo[3,2,1 jk][1,4]benzodiazepin 3 yl] 1h indole 2 carboxamide) 150408-73-4; (ceruletide) 17650-98-5; (n tert butyloxycarbonyltryptophyl[nepsilon (2 methylphenylaminocarbonyl)lysyl]aspartyl n methylphenylalaninamide) 130408-77-4

CN Cam 1481; Fk 480; Ly 219057; Sc 50998; Iqm 95333; Tp 680; T 0632; A 71378; A 71623; Ar r15849; Gw 7178; Gw 5823

L29 ANSWER 91 OF 124 EMBASE on STN

ACCESSION NUMBER: 2000245735 EMBASE

TITLE: A cholecystokinin receptor antagonist blocks milk-induced but not maternal-contact-induced decrease of ultrasonic vocalization in rat pups.

AUTHOR: Weller A.; Gispan I.H.

CORPORATE SOURCE: A. Weller, Developmental Psychobiol. Laboratory, Department of Psychology, Bar Ilan University, Ramat Gan, Israel. weller@mail.biu.ac.il

SOURCE: Developmental Psychobiology, (2000) Vol. 37, No. 1, pp. 35-43.
Refs: 37

ISSN: 0012-1630 CODEN: DEPBA5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000727
Last Updated on STN: 20000727

AB The role of cholecystokinin (CCK) in reducing separation-induced ultrasonic vocalization (USV) was examined by peripheral administration of the selective CCK<SUBA> receptor antagonist devazepide to 10-11-day-old rats. Pups placed alone-for 2min emitted a mean of 55.1 USV/min. When placed on a paper towel wet with warm, sweet milk, USV rate decreased to 23.2/min for the following 8 min. Devazepide (150-600 μg/kg IP) prevented this USV reduction, but did not increase feeding. In contrast, USV reduction produced by contact with the anesthetized dam was not affected by devazepide. Similarly, the opiate antagonist naltrexone (0.5 and 1.0mg/kg) has been shown to block morphine-induced USV decrease in pups away from the dam, but was ineffective when USV reduction was induced by the presence of the dam (Blass et al., 1990; Carden and Hofer, 1990). The current findings suggest that CCK's role is specific, in that it mediates milk- but not daminduced quieting of USV. The results, however, are not incompatible with the possibility that CCK and opioids are part of multiple, redundant pathways that mediate the quieting of USV by the dam. (C) 2000 John Wiley and Sons, Inc.

CT Medical Descriptors:
*vocalization
maternal deprivation
feeding behavior
nonhuman
rat
animal experiment
controlled study
article
Drug Descriptors:
*cholecystokinin receptor: EC, endogenous compound
*devazepide
milk
naltrexone
morphine
RN (devazepide) **103420-77-5**; (milk) 8049-98-7; (naltrexone) 16590-41-3, 16676-29-2; (morphine) 52-26-6, 57-27-2

L29 ANSWER 92 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999088708 EMBASE
TITLE: Cholecystokinin and morphine-induced hypothermia.
AUTHOR: Rezayat M.; Ravandeh N.; Zarrindast M.-R.
CORPORATE SOURCE: M.R. Zarrindast, Department of Pharmacology, School of Medicine, Tehran Univ. Medical Sciences, P.O. Box 13145-784, Tehran, Iran (Islamic Republic of)
SOURCE: European Neuropsychopharmacology, (1999) Vol. 9, No. 3, pp. 219-225.
Refs: 54
ISSN: 0924-977X CODEN: EURNE8
PUBLISHER IDENT.: S 0924-977X(98)00029-7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology

030 Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990319
Last Updated on STN: 19990319

AB The effects of cholecystokinin-8 sulfate (CCK-8), cholecystokinin-8 unsulfate (CCK-8U), cholecystokinin-4 (CCK-4), caerulein and morphine on mice core body temperature have been studied in the present work. Subcutaneous injection of different doses of caerulein (0.05, 0.1 and 0.5 mg/kg), CCK-8 (0.05, 0.1 and 0.25 mg/kg) and morphine (10, 20 and 30 mg/kg) induced hypothermia. CCK-8U and CCK-4 did not elicit any response. The hypothermic response induced by caerulein, a CCK-related decapeptide but not morphine was decreased by selective CCK(A) receptor antagonist MK-329. However, the hypothermia induced by morphine but not caerulein was reduced by opioid antagonist naloxone. When morphine plus caerulein was administered a higher hypothermia was induced. Pretreatment of animals with l-365 260, a selective CCK(B) receptor antagonist did not alter the hypothermia induced by the drugs. The response induced by combination of the both drugs was decreased by MK-329. Administration of CCK antagonists MK-329 and l-365 260 to mice did not exert any effect on temperature. It is concluded that the CCK(A) receptor mechanism may be involved in the hypothermic effect of CCK agonists or morphine, while opioid receptor mechanism is not involved in CCK receptor agonists' response.

CT Medical Descriptors:
*hypothermia: ET, etiology
dose response
nonhuman
male
mouse
animal experiment
controlled study
subcutaneous drug administration
article
priority journal
Drug Descriptors:
***morphine: PD, pharmacology**
***morphine: IT, drug interaction**
***morphine: DO, drug dose**
***morphine: CM, drug comparison**
***morphine: CB, drug combination**
*cholecystokinin derivative: PD, pharmacology
*cholecystokinin derivative: IT, drug interaction
*cholecystokinin derivative: CM, drug comparison
*cholecystokinin derivative: CB, drug combination
ceruletide: PD, pharmacology
ceruletide: IT, drug interaction
ceruletide: DO, drug dose
ceruletide: CM, drug comparison
ceruletide: CB, drug combination
cholecystokinin octapeptide: PD, pharmacology
cholecystokinin octapeptide: IT, drug interaction
cholecystokinin octapeptide: DO, drug dose
cholecystokinin octapeptide: CM, drug comparison
cholecystokinin octapeptide: CB, drug combination
tetragastrin: PD, pharmacology
tetragastrin: IT, drug interaction

tetragastrin: DO, drug dose
tetragastrin: CM, drug comparison
tetragastrin: CB, drug combination
cholecystokinin receptor blocking agent: PD, pharmacology
cholecystokinin receptor blocking agent: IT, drug interaction
cholecystokinin receptor blocking agent: CM, drug comparison
cholecystokinin receptor blocking agent: CB, drug combination
naloxone: PD, pharmacology
naloxone: IT, drug interaction
naloxone: CM, drug comparison
naloxone: CB, drug combination
devazepide: PD, pharmacology
devazepide: IT, drug interaction
devazepide: CM, drug comparison
devazepide: CB, drug combination
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CM, drug comparison
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CB, drug combination

RN (morphine) 52-26-6, 57-27-2; (ceruletide) 17650-98-5; (cholecystokinin octapeptide) 25126-32-3; (tetragastrin) 1947-37-1; (naloxone) 357-08-4, 465-65-6; (devazepide) **103420-77-5**; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0

CN (1) L 365260; (2) Mk 329

CO (2) Merck (United Kingdom); Macfarlan Smith (United Kingdom); Farmitalia Carlo Erba (Italy); Sigma (United States)

L29 ANSWER 93 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999286857 EMBASE
TITLE: Signal transduction in neuropathic pain, with special emphasis on the analgesic role of opioids - Part II: Moving basic science towards a new pharmacotherapy.
AUTHOR: McCormack K.
CORPORATE SOURCE: K. McCormack, Drug Research Group, McCormack Limited, Church House, Church Square, Leighton Buzzard, Beds. LU7 7AE, United Kingdom
SOURCE: Pain Reviews, (1999) Vol. 6, No. 2, pp. 99-131.
Refs: 326
ISSN: 0968-1302 CODEN: PAREFV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990826
Last Updated on STN: 19990826

AB In the first part of this three-part article I explored the notion that pharmacological intervention, aimed at eliminating abnormal sensations such as hyperalgesia or paraesthesia arising as a direct result of nerve injury, activates adaptive responses that ensure adequacy of neurotransmission, regardless of whether such transmission ultimately evokes normal or abnormal sensations. Thus, by their nature, such

adaptive responses will act to oppose and surmount any drug-induced intervention designed to diminish pain through attenuation of signal conduction. A corollary of this hypothesis is that even the most sophisticated novel pharmacological entities, when used to block the pain signal, represent substrates for evoking a repertoire of failsafe mechanisms that have evolved throughout a history of challenge and response. In Part II, I explore in greater depth how activation of these responses may explain why the treatment of neuropathic pains, particularly with opioids, can be so frustrating.

CT Medical Descriptors:
signal transduction
hyperalgesia: CO, complication
hyperalgesia: DT, drug therapy
hyperalgesia: PC, prevention
paresthesia: CO, complication
paresthesia: DT, drug therapy
paresthesia: PC, prevention
nerve injury
neurotransmission
hypothesis
drug design
neuropathy: DT, drug therapy
drug receptor binding
drug potentiation
drug mechanism
human
nonhuman
intracerebroventricular drug administration
intrathecal drug administration
article
Drug Descriptors:
*analgesic agent: CB, drug combination
*analgesic agent: DV, drug development
*analgesic agent: IT, drug interaction
*analgesic agent: PD, pharmacology
*opiate agonist: CB, drug combination
*opiate agonist: IT, drug interaction
*opiate agonist: PD, pharmacology
cholecystokinin b receptor antagonist: CB, drug combination
cholecystokinin b receptor antagonist: DT, drug therapy
cholecystokinin b receptor antagonist: PD, pharmacology
morphine: AD, drug administration
morphine: CB, drug combination
morphine: IT, drug interaction
morphine: PD, pharmacology
buprenorphine: CB, drug combination
buprenorphine: IT, drug interaction
buprenorphine: PD, pharmacology
fentanyl: IT, drug interaction
fentanyl: PD, pharmacology
cholecystokinin: EC, endogenous compound
morphiceptin[3 (n methylphenylalanine) 4 dextro prolinamide]
beta hydroxymefentanyl
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]
proglumide: CB, drug combination
proglumide: PD, pharmacology
devazepide: CB, drug combination
devazepide: PD, pharmacology
lorglumide: CB, drug combination

lorglumide: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: CB, drug combination
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: PD, pharmacology
naloxone
antisense oligonucleotide: CB, drug combination
cam 1481
4 bromo n (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl)benzamide: PD, pharmacology
cholecystokinin b receptor: EC, endogenous compound
cholecystokinin a receptor: EC, endogenous compound
pd 135158: PD, pharmacology
opiate: CB, drug combination
opiate: IT, drug interaction
dynorphin a
cromakalim: CB, drug combination
cromakalim: IT, drug interaction
methadone: CB, drug combination
methadone: IT, drug interaction
levorphanol: IT, drug interaction
potassium channel blocking agent: AD, drug administration
potassium channel blocking agent: IT, drug interaction
gliquidone: IT, drug interaction

RN (morphine) 52-26-6, 57-27-2; (buprenorphine) 52485-79-7, 53152-21-9; (fentanyl) 437-38-7; (cholecystokinin) 9011-97-6, 93443-27-7; (morphiceptin[3 (n methylphenylalanine) 4 dextro prolinamide]) 83397-56-2; (beta hydroxymefentanyl) 78995-14-9; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (proglumide) 6620-60-6; (devazepide) **103420-77-5**; (lorglumide) 97964-56-2; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (naloxone) 357-08-4, 465-65-6; (4 bromo n (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl)benzamide) 111035-59-7; (pd 135158) 130325-35-8; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (dynorphin a) 80448-90-4, 88161-22-2; (cromakalim) 94470-67-4; (methadone) 1095-90-5, 125-56-4, 23142-53-2, 297-88-1, 76-99-3; (levorphanol) 125-72-4, 77-07-6; (gliquidone) 33342-05-1
CN Pl 017; L 365260; Ci 988; Cam 1481; L 365031; Pd 135158

L29 ANSWER 94 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999188465 EMBASE
TITLE: BOC-CCK-4, CCK(B) receptor agonist, antagonizes anxiolytic-like action of morphine in elevated plus-maze.
AUTHOR: Koks S.; Soosaar A.; Voikar V.; Bourin M.; Vasar E.
CORPORATE SOURCE: Dr. S. Koks, Department of Physiology, University of Tartu, 2 Naituse Street, EE2400 Tartu, Estonia. sulev.koks@ut.ee
SOURCE: Neuropeptides, (1999) Vol. 33, No. 1, pp. 63-69.
Refs: 25
ISSN: 0143-4179 CODEN: NRPPDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990701
Last Updated on STN: 19990701

AB This study investigated a role of cholecystokinin (CCK) in the anxiolytic-like action of morphine, an agonist of μ-opioid receptors, in the rat plus-maze model of anxiety. The acute administration of morphine (1 mg/kg) induced a significant increase of exploratory activity in the plus- maze, but did not affect the locomotor activity in the motility test. The higher dose of morphine (2.5 mg/kg) tended to decrease the locomotor activity and, therefore, did not cause the anxiolytic-like action in the plus-maze. The other drugs (naloxone, BOC-CCK-4, L-365,260) and their combinations with morphine (0.5-1 mg/kg) did not affect the locomotor activity of rats. The opioid antagonist naloxone itself (0.5 mg/kg) did not change the exploratory activity in the plus-maze, but potently antagonized the anxiolytic-like action of morphine (1 mg/kg). An agonist of CCK(B) receptors BOC-CCK-4 (1-50 μg/kg) induced a dose-dependent anxiogenic-like action in the plus-maze. Nevertheless, only one dose of BOC-CCK-4 (10 μg/kg) completely reversed the action of morphine. Also, one dose of CCK(B) receptor antagonist L-365,260 (10 μg/kg) was effective to modify the behaviour of rats in the elevated plus-maze. Namely, this dose of L-365,260 increased the ratio between open and total arm entries, a behavioural measure believed to reflect the anxiolytic-like action in the elevated plus-maze. The combination of L-365,260 (100 μg/kg) with the sub-effective dose of morphine (0.5 mg/kg) caused the anxiolytic-like action in the plus-maze not seen if the drugs were given alone. In conclusion, morphine induces a potent anxiolytic-like action in the elevated plus-maze and CCK is acting as an endogenous antagonist of this effect of morphine.

CT Medical Descriptors:
*maze test
drug effect
drug antagonism
tranquilizing activity
locomotion
exploratory behavior
antinociception
anxiety
periaqueductal gray matter
nonhuman
rat
animal experiment
animal model
controlled study
article
priority journal
Drug Descriptors:
*tetragastrin: IT, drug interaction
*tetragastrin: PD, pharmacology
*cholecystokinin b receptor antagonist: IT, drug interaction
*cholecystokinin b receptor antagonist: PD, pharmacology
***morphine: PD, pharmacology**
mu opiate receptor
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
naloxone

n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide: PD, pharmacology
devazepide
RN (tetragastrin) 1947-37-1; (morphine) 52-26-6, 57-27-2; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (naloxone) 357-08-4, 465-65-6; (n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide) 96744-75-1; (devazepide) **103420-77-5**
CN (1) L 365260; U 69593
CO (1) Merck Sharp and Dohme; Boehringer Ingelheim; Sigma

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ACCESSION NUMBER: 97332165 EMBASE
DOCUMENT NUMBER: 1997332165
TITLE: Cholecystokinin inhibits peripheral opioid analgesia in inflamed tissue.
AUTHOR: Schafer M.; Zhou L.; Stein C.
CORPORATE SOURCE: M. Schafer, BPGS, Division of Intramural Research, National Institute on Drug Abuse, Baltimore, MD 21224, United States
SOURCE: Neuroscience, (1998) Vol. 82, No. 2, pp. 603-611.
Refs: 49
ISSN: 0306-4522 CODEN: NRSCDN
PUBLISHER IDENT.: S 0306-4522(97)00304-7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 971204
Last Updated on STN: 971204

AB There is abundant evidence that opioid receptors are present on peripheral terminals of primary afferent neurons. Experimental and clinical studies have shown that activation of these peripheral opioid receptors produces potent analgesia. In addition to peripheral opioid receptors, cholecystokinin receptors are present in sensory neurons. We examined the hypothesis that cholecystokinin receptors may be present on the same primary afferent neuron and that either exogenous or endogenous cholecystokinin may modulate peripheral antinociceptive effects of μ-opioid receptor agonists. Administration of cholecystokinin into inflamed paws, of the rat, but not intravenously attenuated peripheral antinociceptive effects induced by two μ-opioid receptor agonists, [D-Ala2,N-methyl-Phe4,Gly-ol5]-enkephalin and fentanyl. Only the desulphated form of cholecystokinin produced significant and dose-dependent attenuation. Cholecystokinin alone did not alter nociceptive baseline values in inflamed or non-inflamed paws. The anti-opioid effect of cholecystokinin was dose-dependently antagonized by the cholecystokinin(B) receptor-selective antagonist L-365260, but not by the cholecystokinin(A) receptor-selective antagonist L-364718. Local pretreatment with the protein kinase C specific inhibitor calphostin C abolished cholecystokinin's effect. Peripheral antinociceptive effects of [D-Ala2,N- methyl-Phe4,Gly-ol5]-enkephalin and fentanyl were not altered by intraplantar L-365260 alone. These results indicate that activation of peripheral cholecystokinin(B) but not cholecystokinin(A) receptors attenuates the local antinociceptive effects of μ-opioid receptor agonists in inflamed tissue. This anti-opioid effect may be mediated by

protein kinase C in sensory nerve terminals. Endogenous cholecystokinin does not seem to influence the efficacy of peripheral opioids under both normal and inflammatory conditions.

CT Medical Descriptors:
*analgesia
*antinociception
*inflammation
animal experiment
animal model
animal tissue
article
controlled study
intramuscular drug administration
intravenous drug administration
male
muscle spindle afferent nerve
nerve ending
nonhuman
paw edema
plantaris muscle
priority journal
rat
second messenger
sensory nerve cell
Drug Descriptors:
*cholecystokinin: IT, drug interaction
*cholecystokinin: PD, pharmacology
*opiate receptor: EC, endogenous compound
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: IT, drug interaction
calphostin c: PD, pharmacology
calphostin c: IT, drug interaction
cholecystokinin a receptor: EC, endogenous compound
cholecystokinin b receptor: EC, endogenous compound
desulfocholecystokinin octapeptide: PD, pharmacology
desulfocholecystokinin octapeptide: IT, drug interaction
devazepide: PD, pharmacology
devazepide: IT, drug interaction
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: IT, drug interaction
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: PD, pharmacology
fentanyl citrate: PD, pharmacology
fentanyl citrate: IT, drug interaction
mu opiate receptor agonist: PD, pharmacology
mu opiate receptor agonist: IT, drug interaction
protein kinase c: EC, endogenous compound

RN (cholecystokinin) 9011-97-6, 93443-27-7; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (calphostin c) 121263-19-2; (desulfocholecystokinin octapeptide) 25679-24-7; (devazepide) **103420-77-5**; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (fentanyl citrate) 990-73-8; (protein kinase c) 141436-78-4

CN (1) L 364718; (2) L 365260

CO (2) Merck and co (United States); Peninsula (United States); National institute on drug abuse (United States); Calbiochem (United States); Halocarbon (United States)

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ACCESSION NUMBER: 1998100095 EMBASE
TITLE: Cholecystokinin modulates the aversive component of morphine withdrawal syndrome in rats.
AUTHOR: Valverde O.; Roques B.P.
CORPORATE SOURCE: O. Valverde, Dept. de Pharmacochimie Moleculaire, Structurale INSERM U266-CNRS URA, UFR des Sci. Pharmaceut./Biologiques, 4 avenue de l'Observatoire, 75270 Paris Cedex 06, France
SOURCE: Neuroscience Letters, (6 Mar 1998) Vol. 244, No. 1, pp. 37-40.
Refs: 30
ISSN: 0304-3940 CODEN: NELED5
PUBLISHER IDENT.: S 0304-3940(98)00118-9
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 19980507

AB The conditioned place aversion paradigm was used to investigate the role of cholecystokinin in the aversive/dysphoric component of morphine abstinence. Several cholecystokinin ligands were chronically administered during the development of morphine dependence: the CCK(A), antagonist devazepide, the CCK(B) antagonists PD-134,308 and L-365,260, and the CCK(B) agonist BC 264. The CCK-B antagonists L-365,260 and PD-134,308 decreased and completely blocked (respectively) the place aversion induced by naloxone in morphine dependent animals whereas BC 264 and devazepide were inactive in this model. No effect was observed in non-dependent animals after chronic administration of these CCK-ligands. These results show a distinct role for CCK receptors in the regulation of the motivational component of morphine abstinence, probably related to their differential effects in the regulation of limbic dopaminergic neurons.

CT Medical Descriptors:
*withdrawal syndrome: ET, etiology
hormonal regulation
aversion
morphine addiction: ET, etiology
drug effect
nonhuman
male
rat
animal experiment
intraperitoneal drug administration
article
priority journal
Drug Descriptors:
***morphine**
*cholecystokinin
*cholecystokinin receptor
cholecystokinin a receptor antagonist: PD, pharmacology
devazepide: PD, pharmacology
cholecystokinin b receptor antagonist: PD, pharmacology
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2

methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
cholecystokinin receptor stimulating agent: PD, pharmacology
bc 264: PD, pharmacology
unclassified drug

RN (morphine) 52-26-6, 57-27-2; (cholecystokinin) 9011-97-6, 93443-27-7; (devazepide) **103420-77-5**; (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0

CN Pd 134308; L 365260; Bc 264

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ACCESSION NUMBER: 96362037 EMBASE
DOCUMENT NUMBER: 1996362037
TITLE: Association of enkephalin catabolism inhibitors and CCK-B antagonists: A potential use in the management of pain and opioid addiction.
AUTHOR: Roques B.P.; Noble F.
CORPORATE SOURCE: Dept. de Pharmacochimie Moleculaire, INSERM U266-CNRS URA D 1500, Universite Rene Descartes, 4, Avenue de l'Observatoire,75270 Paris Cedex 06, France
SOURCE: Neurochemical Research, (1996) Vol. 21, No. 11, pp. 1397-1410.
ISSN: 0364-3190 CODEN: NEREDZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 961223
Last Updated on STN: 961223

AB The overlapping distribution of opioid and cholecystokinin (CCK) peptides and their receptors (μ and δ opioid receptors; CCK-A and CCK-B receptors) in the central nervous system have led to a large number of studies aimed at clarifying the functional relationships between these two neuropeptides. Most of the pharmacological studies devoted to the role of CCK and enkephalins have been focused on the control of pain. Recently the existence of regulatory mechanisms between both systems have been proposed, and the physiological antagonism between CCK and endogenous opioid systems has been definitely demonstrated by coadministration of CCK-B selective antagonists with RB 101, a systemically active inhibitor, which fully protects enkephalins from their degradation. Several studies have also been done to investigate the functional relationships between both systems in development of opioid side-effects and in behavioral responses. This article will review the experimental pharmacology of association of enkephalin- degrading enzyme inhibitors and CCK-B antagonists to demonstrate the interest of these molecules in the management of both pain and opioid addiction.

CT Medical Descriptors:
*opiate addiction
*pain
analgesia

antinociception
article
drug potentiation
drug tolerance
hot plate test
human
intracerebroventricular drug administration
intraperitoneal drug administration
intravenous drug administration
nonhuman
priority journal
reward
tail flick test
withdrawal syndrome
Drug Descriptors:
*aminopeptidase: EC, endogenous compound
*cholecystokinin b receptor antagonist: PD, pharmacology
*enkephalin: EC, endogenous compound
*enkephalinase inhibitor: PD, pharmacology
*enzyme inhibitor: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine
8 chloro 2,3,4,5 tetrahydro 3 methyl 5 phenyl 1h 3 benzazepin 7 ol hydrogen maleate
bc 264
cholecystokinin: EC, endogenous compound
cholecystokinin receptor stimulating agent
delta opiate receptor: EC, endogenous compound
devazepide
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]
kelatorphan: PD, pharmacology
leucine enkephalin[2 dextro o tert butylserine 6 o tert butylthreonine]
methadone
morphine
n [1 [(2,2 dimethyl 1,3 dioxolan 4 yl)methoxycarbonyl] 2 phenylethyl]phenylalanyl beta alanine
n [2 benzyl 3 [(hydroxyamino)carbonyl]propionyl]phenylalanine: PD, pharmacology
n [3 [(2 amino 4 methylthio)butyldithio] 2 benzylpropionyl]phenylalanine benzyl ester: PD, pharmacology
naloxone
naltrindole
proglumide
thiorphan
unclassified drug

RN (aminopeptidase) 9031-94-1; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (8 chloro 2,3,4,5 tetrahydro 3 methyl 5 phenyl 1h 3 benzazepin 7 ol hydrogen maleate) 87134-87-0; (cholecystokinin) 9011-97-6, 93443-27-7; (devazepide) **103420-77-5**; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (kelatorphan) 92175-57-0; (leucine enkephalin[2 dextro o tert butylserine 6 o tert butylthreonine]) 111035-57-5; (methadone) 1095-90-5, 125-56-4, 23142-53-2, 297-88-1, 76-99-3; (morphine) 52-26-6, 57-27-2; (n [1 [(2,2 dimethyl 1,3 dioxolan 4 yl)methoxycarbonyl] 2 phenylethyl]phenylalanyl beta alanine) 105262-04-2; (n [2 benzyl 3

[(hydroxyamino)carbonyl]propionyl]phenylalanine) 105831-46-7; (n [3 [(2 amino 4 methylthio)butyldithio] 2 benzylpropionyl]phenylalanine benzyl ester) 135949-60-9; (naloxone) 357-08-4, 465-65-6; (naltrindole) 111555-53-4; (proglumide) 6620-60-6; (thiorphan) 76721-89-6

CN Rb 38 a; Rb 101; Bc 264; Pd 134308; Sch 34826; Sch 23390; L 365260; Mk 329

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ACCESSION NUMBER: 96072417 EMBASE
DOCUMENT NUMBER: 1996072417
TITLE: Synthesis, biological evaluation, and quantitative receptor docking simulations of 2-[(acylamino)ethyl]-1,4-benzodiazepines as novel tifluadom- like ligands with high affinity and selectivity for κ-opioid receptors.
AUTHOR: Cappelli A.; Anzini M.; Vomero S.; Menziani M.C.; De Benedetti P.G.; Sbacchi M.; Clarke G.D.; Mennuni L.
CORPORATE SOURCE: Dipartimento di Chimica, Universita degli Studi di Modena, Via Campi 183,41100 Modena, Italy
SOURCE: Journal of Medicinal Chemistry, (1996) Vol. 39, No. 4, pp. 860-872.
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 960319
Last Updated on STN: 960319

AB The synthesis and biological evaluation of a series of 2-substitued 5-phenyl-1,4-benzodiazepines, structurally related to tifluadom (5), the only benzodiazepine that acts simultaneously as a κ-opioid agonist and a cholecystokinin-A (CCK-A) antagonist, are reported. The radioligand binding models used in these studies were [125I](BH)-CCK-8 in rat pancreas (CCK- A), [3H]-(MeNLE28,31)-CCK-8 in guinea pig cerebral cortex (CCK-B), and [3H]U-69593 (κ1), [3H]DAMGO (μ), and [3H]DADLE (δ) in guinea pig brain. All the title compounds were devoid of significant affinity for both CCK-A and CCK-B receptors, while some of them bound with nanomolar affinity and high selectivity for κ-opioid receptors. In particular, the 2-thienyl derivative 7a (X = H) with a K(i) = 0.50 nM represents a clear improvement with respect to tifluadom, showing a comparable potency but higher selectivity. The application of computational simulations and linear regression analysis techniques to the complexes between guinea pig κ (κ1)- receptor and the title compounds allowed the identification of the structural determinants for recognition and quantitative elucidation of the structure affinity relationships in this class of receptors.

CT Medical Descriptors:
*analgesia
*antinociception
animal tissue
article
diuresis
drug screening
drug synthesis
guinea pig
nonhuman
quantitative structure activity relation
rat

receptor affinity
Drug Descriptors:
*benzodiazepine derivative: AN, drug analysis
*benzodiazepine derivative: DV, drug development
*kappa opiate receptor
*opiate agonist: AN, drug analysis
*opiate agonist: DV, drug development
***tifluadom**
2,3 dihydro 1 methyl 5 phenyl 2 [2 [(2 thienylcarbonyl)amino]ethyl] 1h 1,4 benzodiazepine: DV, drug development
2,3 dihydro 1 methyl 5 phenyl 2 [2 [(2 thienylcarbonyl)amino]ethyl] 1h 1,4 benzodiazepine: AN, drug analysis
3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide
4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1 piperazinecarboxylic acid methyl ester
cholecystokinin a receptor
cholecystokinin b receptor
cholecystokinin derivative
cholecystokinin octapeptide
devazepide
enadoline
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]
enkephalin[2 dextro alanine 5 dextro leucine]
lorglumide
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide
naloxone
spiradoline
unclassified drug
RN (tifluadom) 83386-35-0; (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide) 67198-13-4; (4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1 piperazinecarboxylic acid methyl ester) 126766-32-3; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5**; (enadoline) 107431-28-7; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (enkephalin[2 dextro alanine 5 dextro leucine]) 63631-40-3; (lorglumide) 97964-56-2; (n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide) 96744-75-1; (naloxone) 357-08-4, 465-65-6; (spiradoline) 87151-85-7
CN Ci 977; Gr 89696; U 69593; U 50488; U 62066
CO New england nuclear (Italy)

L29 ANSWER 99 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97116846 EMBASE
DOCUMENT NUMBER: 1997116846
TITLE: Involvement of spinal cholecystokinin(B) receptors in mediating neurotensin hyperalgesia from the medullary nucleus raphe magnus in the rat.
AUTHOR: Urban M.O.; Smith D.J.; Gebhart G.F.
CORPORATE SOURCE: Dr. M.O. Urban, Department of Pharmacology, Bowen Science Building, University of Iowa, Iowa City, IA 52242, United States
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1996) Vol. 278, No. 1, pp. 90-96.
Refs: 49
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
024 Anesthesiology

030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970520
Last Updated on STN: 970520

AB Neurotensin microinjection into the medullary nucleus raphe magnus (RMg) has been shown to both inhibit and facilitate the spinal nociceptive tail-flick reflex in a dose-dependent manner. Our study was designed to determine a potential involvement of spinal cholecystokinin octapeptide (CCK) in mediating neurotensin hyperalgesia from the RMg. Microinjection of neurotensin (50 ng) into the RMg of awake rats produced a facilitation of the tail-flick reflex that was completely inhibited by intrathecal (i.t.) administration of the nonselective CCK receptor antagonist proglumide (100 ng). Conversely, injection of a greater dose of neurotensin (5 μg) into the RMg produced an inhibition of the tail-flick reflex that was enhanced by i.t. proglumide. Intrathecal administration of the selective CCK(B) receptor antagonist L-365260 dose-dependently inhibited neurotensin hyperalgesia from the RMg (ID50 = 0.42 ng) at doses approximately 1000-fold less than that observed with the selective CCK(A) receptor antagonist devazepide (ID50 = 646 ng). Injection of CCK alone i.t. produced a biphasic response on the tail-flick reflex as lesser doses (0.1-0.3 ng) inhibited the reflex although greater doses (30-100 ng) facilitated it. Similar to supraspinal neurotensin hyperalgesia, the hyperalgesia observed with i.t. CCK (30 ng) was inhibited by i.t. L-365260 (ID50 = 0.59 ng) at doses approximately 1000-fold less than that observed with i.t. devazepide (ID50 = 630 ng). These data indicate that spinal CCK can both inhibit and facilitate spinal nociceptive responses. The facilitation of nociception observed with spinal CCK appears to involve CCK(B) receptors, which is consistent with the data in our study suggesting that spinal CCK(B) receptors mediate neurotensin hyperalgesia from the RMg via descending neuronal projections.

CT Medical Descriptors:
*antinociception
*hyperalgesia
*raphe magnus nucleus
animal experiment
animal tissue
area under the curve
article
controlled study
dose response
intrathecal drug administration
male
microinjection
nerve projection
nonhuman
priority journal
rat
tail flick test
etiology
Drug Descriptors:
*cholecystokinin a receptor antagonist: AD, drug administration
*cholecystokinin a receptor antagonist: PD, pharmacology
*cholecystokinin a receptor antagonist: IT, drug interaction
*cholecystokinin a receptor antagonist: DO, drug dose
*cholecystokinin b receptor: EC, endogenous compound
*cholecystokinin b receptor antagonist: IT, drug interaction
*cholecystokinin b receptor antagonist: PD, pharmacology

*cholecystokinin b receptor antagonist: AD, drug administration
*cholecystokinin b receptor antagonist: DO, drug dose
*cholecystokinin octapeptide: AD, drug administration
*cholecystokinin octapeptide: PD, pharmacology
*cholecystokinin octapeptide: DO, drug dose
*cholecystokinin octapeptide: IT, drug interaction
*cholecystokinin octapeptide: EC, endogenous compound
*neurotensin: EC, endogenous compound
*neurotensin: PD, pharmacology
*neurotensin: AD, drug administration
*neurotensin: DO, drug dose
*neurotensin: IT, drug interaction
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: IT, drug interaction
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: DO, drug dose
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: AD, drug administration
devazepide: PD, pharmacology
devazepide: IT, drug interaction
devazepide: DO, drug dose
devazepide: AD, drug administration
narcotic analgesic agent: PD, pharmacology
proglumide: IT, drug interaction
proglumide: DO, drug dose
proglumide: AD, drug administration
proglumide: PD, pharmacology

RN (cholecystokinin octapeptide) 25126-32-3; (neurotensin) 39379-15-2; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (devazepide) **103420-77-5**; (proglumide) 6620-60-6
CN (1) L 364718; (2) L 365260
CO (2) Merck sharp and dohme (United Kingdom); Sigma (United States)

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ACCESSION NUMBER: 96251998 EMBASE
DOCUMENT NUMBER: 1996251998
TITLE: The role of cholecystokinin in nociception, neuropathic pain and opiate tolerance.
AUTHOR: Wiesenfeld-Hallin Z.; Xu X.-J.
CORPORATE SOURCE: Dept. Medical Laboratory Sciences, Section Clinical Neurophysiology, Huddinge University Hospital,S-141 86 Huddinge, Sweden
SOURCE: Regulatory Peptides, (1996) Vol. 65, No. 1, pp. 23-28. ISSN: 0167-0115 CODEN: REPPDY
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 960924
Last Updated on STN: 960924

CT Medical Descriptors:
*central nervous system
*drug tolerance

*nociception
*somatosensory system
human
nonhuman
priority journal
review
Drug Descriptors:
*cholecystokinin: EC, endogenous compound
*cholecystokinin receptor: EC, endogenous compound
*cholecystokinin receptor blocking agent: PD, pharmacology
*cholecystokinin receptor blocking agent: DV, drug development
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: DV, drug development
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: DV, drug development
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: PD, pharmacology
devazepide: PD, pharmacology
devazepide: DV, drug development
lorglumide: PD, pharmacology
lorglumide: DV, drug development
ly 262691: PD, pharmacology
ly 262691: DV, drug development
morphine: CB, drug combination
morphine: IT, drug interaction
proglumide: CB, drug combination
proglumide: IT, drug interaction
proglumide: PD, pharmacology
unclassified drug
RN (cholecystokinin) 9011-97-6, 93443-27-7; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (devazepide) **103420-77-5**; (lorglumide) 97964-56-2; (morphine) 52-26-6, 57-27-2; (proglumide) 6620-60-6
CN Mk 329; L 365260; Ci 988; Ly 262691

L29 ANSWER 101 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95262121 EMBASE
DOCUMENT NUMBER: 1995262121
TITLE: Interaction between CCK and opioids in the modulation of the rectocolonic inhibitory reflex in rats.
AUTHOR: Gue M.; Del Rio C.; Junien J.L.; Bueno L.
CORPORATE SOURCE: Dept. of Pharmacology, INRA 180, Chemin de Tournefeuille,31931 Toulouse cedex, France
SOURCE: American Journal of Physiology - Gastrointestinal and Liver Physiology, (1995) Vol. 269, No. 2 32-2, pp. G240-G245. ISSN: 0193-1857 CODEN: APGPDF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950926

Last Updated on STN: 950926

AB The effects of cholecystokinin octapeptide (CCK-8) as well as the involvement of opioid system were evaluated in rectal distension (RD)-induced colonic motor inhibition in rats. Rats were surgically prepared with electrodes implanted on the proximal colon, and a catheter was implanted in lateral ventricle of the brain. RD was performed by inflation (0.0-1.6 ml) of a balloon rectally inserted. RD 1.6 ml of induced an inhibition of the colonic spike bursts (3.1 ± 0.5 per 5 min vs. 8.1 ± 0.4 before RD). Intracerebroventricular but not intravenous injection of CCK-8 and A-71623 (50 and 100 ng/kg) reduced the RD-induced colonic motor inhibition, whereas A-63387 was ineffective. PD-135,158 (10 μg/kg icv) suppressed the inhibitory reflex caused by RD. Devazepide (100 μg/kg icy) had no effect in this reflex function. Devazepide (1 μg/kg), naloxone (0.1 mg/kg), and nor- binaltorphimine (nor-BNI; 10 mg/kg) reversed the blocking effect of CCK-8, whereas PD-135,158 (0.1 μg/kg) and naltrindole (1 mg/kg) have no effect. In conclusion, CCK-8 acts on central alimentary cholecystokinin receptors to modulate the RD-induced inhibition of colonic motility through pathways involving activation of endogenous κ-receptors.

CT Medical Descriptors:
*colon motility
*reflex
*regulatory mechanism
animal experiment
article
ascending colon
binding site
controlled study
electromyogram
male
nonhuman
priority journal
rat
Drug Descriptors:
cholecystokinin receptor
kappa opiate receptor
*cholecystokinin
*cholecystokinin octapeptide
*devazepide
*naloxone
***opiate**
*pd 135158
norbinaltorphimine

RN (cholecystokinin) 9011-97-6, 93443-27-7; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5**; (naloxone) 357-08-4, 465-65-6; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (pd 135158) 130325-35-8; (norbinaltorphimine) 105618-26-6

L29 ANSWER 102 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 94077514 EMBASE
DOCUMENT NUMBER: 1994077514
TITLE: Characterization of SNF 9007, a novel cholecystokinin/opioid ligand in mouse ileum in vitro: Evidence for involvement of cholecystokinin(A) and cholecystokinin(B) receptors in regulation of ion transport.
AUTHOR: Rao R.K.; Levenson S.; Fang S.-N.; Hruby V.J.; Yamamura H.I.; Porreca F.

CORPORATE SOURCE: Department of Pharmacology, Univ. of Arizona College of Medicine,Tucson, AZ 85724, United States
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1994) Vol. 268, No. 2, pp. 1003-1009.
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940414
Last Updated on STN: 940414

AB The effects of cholecystokinin (CCK) fragments and Asp-Tyr-D-Phe-Gly-Trp-[N-Me]Nle-Asp-Phe-NH2 1(SNF 9007), a synthetic CCK analog which binds with high affinity to CCK(B) and opioid delta receptors, were evaluated in isolated sheets of mouse ileum mounted in Ussing flux chambers. Serosal, but not mucosal, administration of cholecystokinin octapeptide-sulfated [CCK8(s)] and cholecystokinin tetrapeptide (30-33) [CCK4(30-33)] produced a brief, concentration-related increase in short circuit current (I(sc)) without changing tissue conductance. Serosal, but not mucosal, SNF 9007 produced a similar concentration-related increase in I(sc) which was followed by an immediate concentration-related and sustained decrease in I(sc); no decrease in I(sc) was observed for either CCK8 or CCK4(30-33). The increase and subsequent decrease in the SNF 9007 I(sc) response were respectively classified as phase I (i.e., CCK-like) and phase II (opioid-like) activity. CCK8(s) and SNF 9007 (phase I) were active at low nanomolar concentrations, whereas CCK4(30-33) was active only at high nanomolar concentrations: the rank order of potencies to increase I(sc) was CCK8(s) > SNF 9007 > CCK4(30- 33). Devazepide (L364,718), a selective antagonist of CCK(A) receptors, effectively blocked the action of CCK8(s), but not that of CCK4(30-33) or SNF 9007 (phase I). In contrast, 3R[+]-N-[2,3-dihydro-1-methyl-2-oxo-5- phenyl-1H-benzodiazepin-3-yl]-N'-[3-methyl-phenyl]urea (L365,260), a selective CCK(B) receptor antagonist, blocked the action of CCK4(30-33) and SNF 9007 (phase I), and also antagonized CCK(B)(s), though to a lesser degree. The phase II response of SNF 9007 was antagonized by N,N-diallyl- Tyr-Aib-Aib-Phe-Leu-OH (ICI 174,864), a selective opioid delta receptor antagonist; this opioid antagonist did not influence the phase I response. Neither L364,718 or L365,260 influenced the SNF 9007 phase II response. Serosal pretreatment of tissues with tetrodotoxin, or the ganglionic blocker chlorisondamine, significantly blocked the actions of CCK8(s) and CCK4(30- 33), and both phase I and phase II responses to SNF 9007. Further, these peptides produced no significant response in mucosal preparations of ileum physically stripped of the enteric ganglia and muscularis externa. The data suggest that ileal ion-transport can be modulated by the activation of neural CCK(A) or CCK(B) receptors which are located partly preganglionically and that these receptors can be selectively activated by derivatives or analogs of CCK. CCK8(s) appears to produce its effects predominately, but not exclusively, at the CCK(A) receptor, whereas SNF 9007 and CCK4(30-33) selectively activate CCK(B) receptors in mouse ileum; SNF 9007 (phase I) is several-fold more potent than CCK4(30-33) in influencing ion transport at the CCK(B) receptor. Finally, SNF 9007 has the unusual profile of acting at opioid delta receptors to produce a subsequent decrease in I(sc). These data demonstrate the importance of both CCK(A) and CCK(B), as well as opioid delta, receptors in the regulation of ion transport in the same intestinal segment.

CT Medical Descriptors:
*ion transport

animal experiment
animal model
animal tissue
article
feedback system
ligand binding
male
mouse
nonhuman
pancreas islet cell
priority journal
receptor affinity
Drug Descriptors:
*cholecystokinin a receptor
*cholecystokinin b receptor
*opiate receptor
delta opiate receptor
neurotransmitter receptor
*cholecystokinin octapeptide
***opiate**
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
aspartyltyrosyl dextro phenylalanylglycyltryptophyl(n methylnorleucyl)aspartylphenylalaninamide: PD, pharmacology
chlorisondamine: PD, pharmacology
devazepide: PD, pharmacology
n,n diallyltyrosyl 2 methylalanyl 2 methylalanylphenylalanylleucine
snf 9007
unclassified drug

RN (cholecystokinin octapeptide) 25126-32-3; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (chlorisondamine) 69-27-2; (devazepide) **103420-77-5**; (n,n diallyltyrosyl 2 methylalanyl 2 methylalanylphenylalanylleucine) 89352-67-0

CN Snf 9007; Ici 174864; L 364718; L 365260

CO Sigma (United States); Peninsula (United States); Cambridge (United States); Merck sharp and dohme (United States)

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ACCESSION NUMBER: 94122823 EMBASE
DOCUMENT NUMBER: 1994122823
TITLE: Recent advances in opioid and non-opioid analgesia (1992-1993).
AUTHOR: Press J.B.; Raffa R.B.
CORPORATE SOURCE: RW Johnson Pharm. Research Institute, Welsh and McKean Roads,Spring House, PA 19477-0776, United States
SOURCE: Expert Opinion on Therapeutic Patents, (1994) Vol. 4, No. 4, pp. 379-393.
ISSN: 0962-2594 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 940504

Last Updated on STN: 940504

CT Medical Descriptors:
*analgesia
antinociception
antioxidant activity
brain ischemia
clinical trial
constipation: SI, side effect
drug absorption
drug mechanism
dysphoria: SI, side effect
enzyme inhibition
human
intraperitoneal drug administration
ion channel
migraine: DT, drug therapy
nonhuman
pain: DT, drug therapy
respiration depression: SI, side effect
review
rheumatic disease: DT, drug therapy
second messenger
serotonin uptake
Drug Descriptors:
adenosine receptor
adrenergic receptor
cholecystokinin receptor
delta opiate receptor
dopamine receptor
kappa opiate receptor
mu opiate receptor
n methyl dextro aspartic acid receptor
opiate receptor
receptor subtype
tachykinin receptor
2 benzhydryl 3 (2 methoxybenzylamino) 1 azabicyclo[2.2.2]octane: DV, drug development
2 benzhydryl 3 (2 methoxybenzylamino) 1 azabicyclo[2.2.2]octane: PD, pharmacology
benzodiazepine derivative: PD, pharmacology
benzodiazepine derivative: DV, drug development
benzodiazepine derivative: AN, drug analysis
benzofuran derivative: DV, drug development
benzofuran derivative: PD, pharmacology
bradykinin antagonist: PD, pharmacology
bradykinin antagonist: PK, pharmacokinetics
bradykinin antagonist: AN, drug analysis
bradykinin antagonist: CT, clinical trial
bradykinin antagonist: DT, drug therapy
4 [alpha (4 allyl 2,5 dimethyl 1 piperazinyl) 3 hydroxybenzyl] n,n diethylbenzamide: DV, drug development
4 [alpha (4 allyl 2,5 dimethyl 1 piperazinyl) 3 hydroxybenzyl] n,n diethylbenzamide: PD, pharmacology
cannabinoid derivative: PD, pharmacology
cannabinoid derivative: DV, drug development
cholecystokinin: DV, drug development
cholecystokinin: PD, pharmacology
cholecystokinin receptor blocking agent: PD, pharmacology
cholecystokinin receptor blocking agent: CT, clinical trial

cholecystokinin receptor blocking agent: DT, drug therapy
cholinergic receptor stimulating agent: DV, drug development
cholinergic receptor stimulating agent: PD, pharmacology
cholinesterase inhibitor: PD, pharmacology
cholinesterase inhibitor: DV, drug development
clonidine derivative: PD, pharmacology
clonidine derivative: DT, drug therapy
devazepide: CT, clinical trial
devazepide: AN, drug analysis
devazepide: DT, drug therapy
devazepide: PD, pharmacology
dextro arginylbradykinin[3 hydroxyproline 7 dextro phenylalanine]: PD, pharmacology
dextro arginylbradykinin[3 hydroxyproline 7 dextro phenylalanine]: CT, clinical trial
dextro arginylbradykinin[3 hydroxyproline 7 dextro phenylalanine]: AN, drug analysis
dextro arginylbradykinin[3 hydroxyproline 7 dextro phenylalanine]: DT, drug therapy
dopamine receptor blocking agent: PD, pharmacology
dopamine receptor blocking agent: AN, drug analysis
dopamine receptor blocking agent: DV, drug development
enkephalinase inhibitor: DT, drug therapy
enkephalinase inhibitor: AE, adverse drug reaction
enkephalinase inhibitor: PD, pharmacology
enkephalinase inhibitor: PK, pharmacokinetics
morphinan derivative: DV, drug development
morphinan derivative: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DV, drug development
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
nonsteroid antiinflammatory agent: PD, pharmacology
nonsteroid antiinflammatory agent: DT, drug therapy
opiate agonist: CT, clinical trial
opiate agonist: DT, drug therapy
opiate agonist: PD, pharmacology
opiate agonist: AE, adverse drug reaction
oxime derivative: AN, drug analysis
oxime derivative: DV, drug development
oxime derivative: PD, pharmacology
prostaglandin receptor blocking agent: PD, pharmacology
prostaglandin receptor blocking agent: DV, drug development
prostaglandin receptor blocking agent: AN, drug analysis
pyrrolidine derivative: PD, pharmacology
pyrrolidine derivative: DV, drug development
serotonin agonist: PD, pharmacology
serotonin agonist: DV, drug development
serotonin antagonist: PD, pharmacology
serotonin antagonist: DT, drug therapy
serotonin antagonist: AN, drug analysis
serotonin uptake inhibitor: PD, pharmacology
serotonin uptake inhibitor: DV, drug development
spiradoline: DT, drug therapy
spiradoline: AE, adverse drug reaction
spiradoline: CT, clinical trial
spiradoline: PD, pharmacology
substance p antagonist: DV, drug development
substance p antagonist: PD, pharmacology
tramadol: PD, pharmacology

tramadol: DT, drug therapy
unindexed drug
RN (2 benzhydryl 3 (2 methoxybenzylamino) 1 azabicyclo[2.2.2]octane) 132746-60-2, 134731-58-1; (4 [alpha (4 allyl 2,5 dimethyl 1 piperazinyl) 3 hydroxybenzyl] n,n diethylbenzamide) 155836-52-5; (cholecystokinin) 9011-97-6, 93443-27-7; (devazepide) **103420-77-5**; (dextro arginylbradykinin[3 hydroxyproline 7 dextro phenylalanine]) 109333-26-8; (spiradoline) 87151-85-7; (tramadol) 27203-92-5, 36282-47-0
CN (1) U 62066; (2) Cp 96345; (3) Npc 567; (4) Mk 329; (5) Bw 373u86
CO (1) Upjohn; (2) Pfizer; (3) Scios nova; (4) Merck sharp and dohme; (5) Burroughs wellcome; Alkaloida chemical works; Ciba geigy; Schering; Merrell dow pharmaceuticals; Mcneil pharmaceuticals; Du pont merck; Rhone poulenc rorer; Toray; Parke davis; Fujisawa; Aesculapius farmaceutici; Glaxo; Novo nordisk; Astra; Smith kline beecham; Takeda chemical industries; Bristol myers squibb; Boots; Sterling winthrop; Yissum; Allergan; Searle

L29 ANSWER 104 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94311087 EMBASE
DOCUMENT NUMBER: 1994311087
TITLE: Diversity of agents that modify opioid tolerance, physical dependence, abstinence syndrome, and self-administrative behavior.
AUTHOR: Bhargava H.N.
CORPORATE SOURCE: Pharmaceutics/Pharmacodynamics Dept., College of Pharmacy, University of Illinois, 833 South Wood Street,Chicago, IL 60612, United States
SOURCE: Pharmacological Reviews, (1994) Vol. 46, No. 3, pp. 293-324.
ISSN: 0031-6997 CODEN: PAREAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
ENTRY DATE: Entered STN: 941102
Last Updated on STN: 941102
CT Medical Descriptors:
*opiate addiction
*pain assessment: DT, drug therapy
*withdrawal syndrome
dose response
drug antagonism
drug formulation
drug structure
drug tolerance
human
neurotransmitter release
nonhuman
priority journal
review
second messenger
self medication
Drug Descriptors:
opiate receptor
receptor subtype
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide

methanesulfonate: CM, drug comparison
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate: AN, drug analysis
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate: PD, pharmacology
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate: TO, drug toxicity
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate: IT, drug interaction
*3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate: DO, drug dose
*cholecystokinin: PD, pharmacology
*decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid: TO, drug toxicity
*decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid: PD, pharmacology
*decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid: IT, drug interaction
*decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid: CM, drug comparison
*decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid: AN, drug analysis
***diamorphine: TO, drug toxicity**
*melanostatin: PD, pharmacology
*melanostatin: AN, drug analysis
***methadone: PD, pharmacology**
***morphine: IT, drug interaction**
***morphine: TO, drug toxicity**
***morphine: PR, pharmaceutics**
***morphine: DT, drug therapy**
***morphine: PD, pharmacology**
***morphine: DO, drug dose**
*naltrindole: AN, drug analysis
*naltrindole: IT, drug interaction
***opiate: EC, endogenous compound**
*protirelin: PD, pharmacology
*protirelin: DO, drug dose
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
buprenorphine: DO, drug dose
buprenorphine: AN, drug analysis
buprenorphine: PD, pharmacology
butorphanol tartrate: PD, pharmacology
butorphanol tartrate: AN, drug analysis
cannabis: TO, drug toxicity
clonidine: PD, pharmacology
devazepide: PD, pharmacology
dizocilpine: IT, drug interaction
dizocilpine: PD, pharmacology
dizocilpine: DO, drug dose
dizocilpine: CM, drug comparison
dizocilpine: AN, drug analysis
dizocilpine: TO, drug toxicity
dynorphin derivative: AN, drug analysis
dynorphin derivative: PD, pharmacology
dynorphin derivative: TO, drug toxicity
enkephalinase inhibitor: PD, pharmacology
enkephalinase inhibitor: AN, drug analysis
ginseng: DO, drug dose

ibogaine: TO, drug toxicity
ibogaine: AN, drug analysis
interferon
levacetylmethadol: PD, pharmacology
levallorphan
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide: AN, drug analysis
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide: PD, pharmacology
naloxone: PD, pharmacology
naloxone: AN, drug analysis
naloxone: IT, drug interaction
naltrexone: AN, drug analysis
naltrexone: DO, drug dose
naltrexone: IT, drug interaction
naltrexone: PD, pharmacology
nitric oxide synthase inhibitor: AN, drug analysis
nitric oxide synthase inhibitor: PD, pharmacology
proglumide: PD, pharmacology
spiradoline: AN, drug analysis
spiradoline: PD, pharmacology
unindexed drug

RN (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate) 83913-06-8; (cholecystokinin) 9011-97-6, 93443-27-7; (decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid) 136109-04-1, 137433-06-8; (diamorphine) 1502-95-0, 561-27-3; (melanostatin) 9083-38-9; (methadone) 1095-90-5, 125-56-4, 23142-53-2, 297-88-1, 76-99-3; (morphine) 52-26-6, 57-27-2; (naltrindole) 111555-53-4; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (protirelin) 24305-27-9; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (buprenorphine) 52485-79-7, 53152-21-9; (butorphanol tartrate) 58786-99-5; (cannabis) 8001-45-4, 8063-14-7; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (devazepide) **103420-77-5**; (dizocilpine) 77086-21-6; (ibogaine) 83-74-9; (levacetylmethadol) 34433-66-4; (levallorphan) 13075-35-9, 152-02-3; (n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide) 96744-75-1; (naloxone) 357-08-4, 465-65-6; (naltrexone) 16590-41-3, 16676-29-2; (proglumide) 6620-60-6; (spiradoline) 87151-85-7

CN Heroin; Mk 801; Ly 274614; U 50488h; Temgesic; Stadol; U 69593; U 62066; L 365260; L 364718

L29 ANSWER 105 OF 124 EMBASE on STN

ACCESSION NUMBER: 94280827 EMBASE
DOCUMENT NUMBER: 1994280827
TITLE: Pharmacological properties of ureido-acetamides, new potent and selective non-peptide CCK(B)/gastrin receptor antagonists.
AUTHOR: Bertrand P.; Bohme G.A.; Durieux C.; Guyon C.; Capet M.; Jeantaud B.; Boudeau P.; Ducos B.; Pendley C.E.; Martin G.E.; Floch A.; Doble A.
CORPORATE SOURCE: Rhone-Poulenc Rorer SA, Ctr. Recherches de Vitry-Alfortville, 13 quai Jules Guesde,94403 Vitry-Sur-Seine Cedex, France
SOURCE: European Journal of Pharmacology, (1994) Vol. 262, No. 3, pp. 233-245.
ISSN: 0014-2999 CODEN: EJPHAZ
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology
003 Endocrinology
023 Nuclear Medicine
029 Clinical Biochemistry
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 941006
Last Updated on STN: 941006

AB We present here the pharmacological properties of 3 ureido-acetamide members of a novel family of non-peptide cholecystokinin-B (CCK(B)) receptor antagonists. RP 69758 (3-{3-[N-(N-methyl N-phenyl-carbamoylmethyl) N-phenylcarbamoylmethyl] ureido) phenylacetic acid), RP 71483 ((E)-2-[3-(3-hydroxyiminomethyl phenyl) ureido] N-(8-quinolyl) N-[(1,2,3,4-tetrahydro 1-quinolyl) carbonylmethyl] acetamide) and RP 72540 ((RS)-2-(3-{3-[N-(3-methoxy phenyl) N-(N-methyl N-phenyl-carbamoylmethyl) carbamoylmethyl] ureido) phenyl) propionic acid) displayed nanomolar affinity for guinea-pig, rat and mouse CCK(B) receptors labelled with [3H]pCCK-8 or with the selective CCK(B) receptor ligand [3H]pBC264. RP 69758 and RP 72540 showed selectivity factors in excess of 200 for CCK(B) versus CCK(A) receptors. All three compounds had also high affinity for gastrin binding sites in the stomach. The ureido-acetamides behaved as potent antagonists of CCK-8-induced neuronal firing in rat hippocampal slices in vitro, a functional model of brain CCK(B) receptor mediated responses. RP 69758 is also a potent gastrin receptor antagonist in vivo that dose dependently inhibits gastric acid secretion induced by i.v. injection of pentagastrin in the rat. None of the three ureido-acetamides, at concentrations up to 1 μM, significantly blocked CCK-8-evoked contractions of the guinea-pig ileum in vitro, a CCK(A) receptor bioassay. In ex vivo binding studies, i.p. administration of RP 69758 and RP 72540 resulted in a dose-dependent inhibition of [3H]pCCK-8 binding in mouse brain homogenate. However, the relative penetration of these ureido-acetamides into the forebrain after peripheral administration was below 0.01%. RP 71483 did not appear to cross the blood-brain barrier in quantities sufficient to prevent [3H]pCCK-8 binding at low doses, a property that makes it suitable for the exploration of the peripheral versus central origin of the behavioural effects observed following systemic administration of CCK. RP 69758, RP 71483 and RP 72540 are highly potent and selective non-peptide CCK(B) receptor antagonists which are useful tools to explore the physiological functions of CCK(B) receptors.

CT Medical Descriptors:
*brain
*stomach acid secretion
animal experiment
animal tissue
article
blood brain barrier
brain slice
controlled study
drug receptor binding
guinea pig
hippocampus
ileum
intravenous drug administration
male
mouse

nonhuman
pancreas
priority journal
rat
single unit activity
Drug Descriptors:
*cholecystokinin b receptor
*gastrin receptor
*cholecystokinin octapeptide: PD, pharmacology
*cholecystokinin receptor blocking agent: PD, pharmacology
*cholecystokinin receptor blocking agent: DO, drug dose
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: PD, pharmacology
bc 264: PD, pharmacology
bradykinin: PD, pharmacology
cholecystokinin derivative: PD, pharmacology
devapamil: PD, pharmacology
devazepide: PD, pharmacology
ethylketazocine: PD, pharmacology
gastrin 17: PD, pharmacology
ketanserin: PD, pharmacology
mepyramine: PD, pharmacology
neuropeptide y: PD, pharmacology
neurotensin: PD, pharmacology
paroxetine: PD, pharmacology
phentolamine: PD, pharmacology
prazosin: PD, pharmacology
preclamol: PD, pharmacology
quinuclidinyl benzilate: PD, pharmacology
radioligand
rp 69758: DO, drug dose
rp 69758: PD, pharmacology
rp 71483: DO, drug dose
rp 71483: PD, pharmacology
rp 72540: DO, drug dose
rp 72540: PD, pharmacology
somatostatin: PD, pharmacology
spiperone: PD, pharmacology
substance p: PD, pharmacology
sulpiride: PD, pharmacology
unindexed drug
vasoactive intestinal polypeptide: PD, pharmacology
unclassified drug
RN (cholecystokinin octapeptide) 25126-32-3; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (bradykinin) 58-82-2, 5979-11-3; (devapamil) 92302-55-1; (devazepide) **103420-77-5**; (ethylketazocine) 36292-66-7; (gastrin 17) 60748-06-3; (ketanserin) 74050-98-9; (mepyramine) 6036-95-9, 91-84-9; (neuropeptide y) 82785-45-3, 83589-17-7; (neurotensin) 39379-15-2; (paroxetine) 61869-08-7; (phentolamine) 50-60-2, 73-05-2; (prazosin) 19216-56-9, 19237-84-4; (preclamol) 75240-91-4, 85966-89-8; (quinuclidinyl benzilate) 6581-06-2; (somatostatin) 38916-34-6, 51110-01-1; (spiperone) 749-02-0; (substance p) 33507-63-0; (sulpiride) 15676-16-1; (vasoactive intestinal polypeptide) 37221-79-7

CN (2) Rp 69758; (4) Rp 72540; (6) Rp 71483; (8) L 365260; (10) Ci 988; Bc 264
CO (9) Rhone poulenc rorer; (10) Rhone poulenc rorer (France); Crb (United Kingdom); Sigma (United States); Amersham (United Kingdom); Du pont new england nuclear (United States)

L29 ANSWER 106 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94009891 EMBASE
DOCUMENT NUMBER: 1994009891
TITLE: Current conservative treatment of acute pancreatitis: Evidence from animal and human studies.
AUTHOR: Niederau C.; Schulz H.-U.
CORPORATE SOURCE: Department of Gastroenterology, Heinrich-Heine-University Dusseldorf, Postfach 10 10 07,40001 Dusseldorf, Germany
SOURCE: Hepato-Gastroenterology, (1993) Vol. 40, No. 6, pp. 538-549.
ISSN: 0172-6390 CODEN: HEGAD4
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940130
Last Updated on STN: 940130

AB Primary treatment of patients suffering from acute pancreatitis is conservative, irrespective of its etiology and initial severity. There is no effective specific therapy for treating the underlying disease process. As a result, the current therapeutic approach involves the provision of supportive care, the elimination of causal (biliary tract) disease, and the treatment of complications. Since complications may develop at any time, patients with moderate or severe disease should be admitted to an intensive care unit for interdisciplinary assessment and constant observation of their clinical status and computed tomography findings. Basic therapy should include total fasting, replacement of deficits in volume, electrolyte and albumin, as well as adequate analgesia. Depending on the patient's specific clinical condition, nasogastric suction, respiratory support, antibiotics, insulin and heparin may become necessary. The use of enzyme inhibitors and drugs capable of inhibiting pancreatic exocrine secretion has not proved effective in clinical trials. The value of prostaglandins, non-steroidal anti-inflammatory drugs and cholecystokinin receptor antagonists remains to be established. Early endoscopic retrograde cholangiopancreatography should be performed in patients with suspected underlying biliary disease Papillotomy should be carried out only when calculi are present in the common bile duct. Local complications, such as pseudocysts and abscesses can often be treated by ultrasound- or CT-guided aspiration and drainage. However, when bacterial infection of pancreatic necrosis becomes evident, surgical intervention should be considered. Future evaluation of new therapeutic approaches by controlled studies needs to include a sufficient number of patients with severe acute pancreatitis.

CT Medical Descriptors:
*acute pancreatitis: DI, diagnosis
*acute pancreatitis: DT, drug therapy
*acute pancreatitis: TH, therapy
*conservative treatment
analgesia
artificial ventilation

biliary tract disease
blood volume
clinical feature
computer assisted tomography
diet restriction
disease severity
electrolyte balance
endoscopic retrograde cholangiopancreatography
human
nonhuman
pain: CO, complication
pain: DT, drug therapy
pancreas abscess: CO, complication
pancreas abscess: TH, therapy
pancreas pseudocyst: CO, complication
pancreas pseudocyst: TH, therapy
pancreas secretion
parenteral nutrition
peritoneum lavage
plasmapheresis
priority journal
review
stomach intubation
Drug Descriptors:
albumin: EC, endogenous compound
antibiotic agent: DT, drug therapy
aprotinin: DT, drug therapy
benzotript: DT, drug therapy
bupivacaine: DT, drug therapy
buprenorphine: DT, drug therapy
calcitonin: DT, drug therapy
camostat mesilate: DT, drug therapy
cholecystokinin receptor blocking agent: DT, drug therapy
cimetidine: DT, drug therapy
devazepide: DT, drug therapy
gabexate mesilate: DT, drug therapy
glucagon: DT, drug therapy
indometacin: DT, drug therapy
insulin: DT, drug therapy
lidocaine: DT, drug therapy
lorglumide: DT, drug therapy
loxiglumide: DT, drug therapy
n tert butyloxycarbonylcholecystokinin[27-32][28,31 norleucine] phenethyl ester: DT, drug therapy
nafamstat mesilate
nonsteroid antiinflammatory agent: DT, drug therapy
pancreas enzyme: EC, endogenous compound
pancreas polypeptide: DT, drug therapy
pentazocine: DT, drug therapy
pirenzepine: DT, drug therapy
procaine: DT, drug therapy
proglumide: DT, drug therapy
prostaglandin: DT, drug therapy
somatostatin: DT, drug therapy
tomoglumide: DT, drug therapy
unindexed drug: DT, drug therapy
RN (aprotinin) 11004-21-0, 12407-79-3, 50936-63-5, 52229-70-6, 58591-29-0, 9050-74-2, 9075-10-9, 9087-70-1; (benzotript) 39544-74-6; (bupivacaine) 18010-40-7, 2180-92-9, 55750-21-5; (buprenorphine) 52485-79-7, 53152-21-9;

(calcitonin) 12321-44-7, 21215-62-3, 9007-12-9; (camostat mesilate) 59721-29-8; (cimetidine) 51481-61-9, 70059-30-2; (devazepide) **103420-77-5**; (gabexate mesilate) 56974-61-9; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (insulin) 9004-10-8; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (lorglumide) 97964-56-2; (loxiglumide) 107097-80-3; (n tert butyloxycarbonylcholecystokinin[27-32][28,31 norleucine] phenethyl ester) 119733-42-5; (nafamstat mesilate) 82956-11-4; (pancreas polypeptide) 59763-91-6; (pentazocine) 359-83-1, 64024-15-3; (pirenzepine) 28797-61-7, 29868-97-1; (procaine) 51-05-8, 59-46-1; (proglumide) 6620-60-6; (somatostatin) 38916-34-6, 51110-01-1; (tomoglumide) 97964-54-0

CN Cr 1409; Cr 1505; Cr 1392; L 364,718; Cck jmv 180; Trasylol; Foy 305; Foy; Fut 175

L29 ANSWER 107 OF 124 EMBASE on STN

ACCESSION NUMBER: 93051125 EMBASE
DOCUMENT NUMBER: 1993051125
TITLE: BRL 46470A: A highly potent, selective and long acting 5-HT3 receptor antagonist with anxiolytic-like properties.
AUTHOR: Blackburn T.P.; Baxter G.S.; Kennett G.A.; King F.D.; Piper D.C.; Sanger G.J.; Thomas D.R.; Upton N.; Wood M.D.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, Coldharbour Road,Harlow, Essex CM19 5AD, United Kingdom
SOURCE: Psychopharmacology, (1993) Vol. 110, No. 3, pp. 257-264. ISSN: 0033-3158 CODEN: PSCHDL
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 023 Nuclear Medicine
029 Clinical Biochemistry
032 Psychiatry
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 930314
Last Updated on STN: 930314

AB The novel 5-HT3 antagonist, BRL 46470A (endo-N-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)2,3-dihydro-3,3 dimethyl-indole-1-carboxamide, hydrochloride), has been investigated in a series of in vitro and in vivo tests, including the effect of the drug in models of anxiolysis. In classical tests for 5-HT3 receptor antagonism, BRL 46470A was shown to antagonise 5-HT3 mediated responses in the guinea-pig ileum [pA2 8.3 ± 0.5, slope 0.98 ± 0.20, mean ± SEM (5)], the rabbit isolated heart (pA2 10.1 ± 0.1, slope 1.2 ± 0.2, n = 5) and the rat Bezold-Jarisch model (ID50 0.7 μg/kg IV ± 0.1, n = 8), with a long duration of action (> 3 h). BRL 46470A selectively displaced [3H]-BRL 43694 from 5-HT3 binding sites in rat brain membranes (K(i) 0.32 nM ± 0.04, n = 4) without displacing (at concentrations greater than 1 μM) a wide variety of ligands binding to other neurotransmitter receptors, opioid receptors and to neurotransmitter gated ion channel complexes. In vivo, BRL 46470A showed anxiolytic-like activity in two animal models predictive of antianxiety effects-elevated X-maze and social interaction in rats. In both models, BRL 46470A showed significant activity over a wide dose-range following both oral (0.0001-0.1 mg/kg PO) and systemic administration. The unique level of potency of BRL 46470A was apparent in the rat social interaction test and was shown to be 100 fold more potent than the 5-HT3 receptor antagonist ondansetron, with no evidence of a bell-shaped dose response curve over 4 orders of magnitude. BRL 46470A (0.0001 and 0.01 mg/kg SC) also reduced the anxiogenic effects of m-CPP (1-(3-chlorophenyl)

piperazine) in the rat elevated X-maze. BRL 46470A is therefore a chemically novel potent and selective 5-HT3 receptor antagonist with anxiolytic potential and a long duration of action in animal studies.

CT Medical Descriptors:
*anxiety
*behavior
animal experiment
animal model
animal tissue
article
blood pressure
brain
controlled study
drug antagonism
esophagus
guinea pig
heart
heart rate
ileum
intraperitoneal drug administration
intravenous drug administration
ligand binding
male
maze test
nonhuman
oral drug administration
priority journal
rabbit
rat
social behavior
subcutaneous drug administration
Drug Descriptors:
*serotonin 3 receptor
*anxiolytic agent: PD, pharmacology
*anxiolytic agent: IT, drug interaction
*anxiolytic agent: DO, drug dose
*serotonin: DO, drug dose
*serotonin: IT, drug interaction
*serotonin: PD, pharmacology
*serotonin antagonist: IT, drug interaction
*serotonin antagonist: PD, pharmacology
*serotonin antagonist: DO, drug dose
(3 chlorophenyl)piperazine: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1,1 dimethyl 4 phenylpiperazinium: PD, pharmacology
2 dipropylamino 8 hydroxytetralin: PD, pharmacology
ricasetron: IT, drug interaction
ricasetron: PD, pharmacology
ricasetron: DO, drug dose
cyanoiodopindolol: PD, pharmacology
devazepide: PD, pharmacology
diazepam: PD, pharmacology
domperidone: PD, pharmacology
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: PD, pharmacology
enkephalin[2 dextro alanine 5 dextro leucine]: PD, pharmacology
ethylketazocine: PD, pharmacology
granisetron: PD, pharmacology

idazoxan: PD, pharmacology
mesulergine: PD, pharmacology
mianserin: PD, pharmacology
nicotine: PD, pharmacology
ondansetron: PD, pharmacology
oxotremorine m: PD, pharmacology
pizotifen: PD, pharmacology
prazosin: PD, pharmacology
quinuclidinyl benzilate: PD, pharmacology
radioligand
strychnine: PD, pharmacology
tert butylbicyclophosphorothioate: PD, pharmacology
unindexed drug

RN (serotonin) 50-67-9; ((3 chlorophenyl)piperazine) 6640-24-0; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (1,1 dimethyl 4 phenylpiperazinium) 114-28-3, 29721-66-2; (2 dipropylamino 8 hydroxytetralin) 78950-78-4; (ricasetron) 117086-68-7; (cyanoiodopindolol) 83498-72-0; (devazepide) **103420-77-5**; (diazepam) 439-14-5; (domperidone) 57808-66-9; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (enkephalin[2 dextro alanine 5 dextro leucine]) 63631-40-3; (ethylketazocine) 36292-66-7; (granisetron) 107007-99-8, 109889-09-0; (idazoxan) 79944-56-2, 79944-58-4; (mesulergine) 64795-35-3, 72786-12-0; (mianserin) 21535-47-7, 24219-97-4; (nicotine) 54-11-5; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (oxotremorine m) 63939-65-1; (pizotifen) 15574-96-6; (prazosin) 19216-56-9, 19237-84-4; (quinuclidinyl benzilate) 6581-06-2; (strychnine) 1421-86-9, 57-24-9; (tert butylbicyclophosphorothioate) 70636-86-1

CN (1) Brl 46470a; (2) L 364718; (3) L 365260; (4) Brl 43694

CO (1) Smith kline beecham (United Kingdom); (4) New england nuclear; Sigma; Rbi; Courtin and warner (United Kingdom); Amersham

L29 ANSWER 108 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 93208063 EMBASE
DOCUMENT NUMBER: 1993208063
TITLE: Toward peptide receptor ligand drugs: Progress on nonpeptides.
AUTHOR: Freidinger R.M.
CORPORATE SOURCE: Medicinal Chemistry Department, Merck Research Laboratories,West Point, PA 19486, United States
SOURCE: Progress in Drug Research, (1993) Vol. 40, pp. 33-98. ISSN: 0071-786X CODEN: FAZMAE
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 930822
Last Updated on STN: 930822

CT Medical Descriptors:
*renin angiotensin aldosterone system
drug receptor binding
human
nonhuman
review
Drug Descriptors:

*cholecystokinin receptor
*opiate receptor
receptor subtype
*cholecystokinin derivative: DV, drug development
*cholecystokinin receptor blocking agent: DV, drug development
*neurokinin: DV, drug development
***opiate: DV, drug development**
*opiate antagonist: DV, drug development
3,4 dichloro n methyl n [1 phenyl 2 (1 pyrrolidinyl)ethyl]benzeneacetamide
: DV, drug development
8 [(3,4 dichlorophenyl)acetyl] 7 (1 pyrrolidinylmethyl) 1,4 dioxa 8
azaspiro[4.5]decane: DV, drug development
asperlicin: DV, drug development
benzotript: DV, drug development
beta funaltrexamine: DV, drug development
butorphanol: DV, drug development
devazepide: DV, drug development
ethylketazocine: DV, drug development
fentanyl: DV, drug development
lorglumide: DV, drug development
loxiglumide: DV, drug development
meptazinol: DV, drug development
morphine: DV, drug development
n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzo[b]thiophene 4 acetamide:
DV, drug development
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide:
DV, drug development
naloxone: DV, drug development
naltrindole: DV, drug development
norbinaltorphimine: DV, drug development
pethidine: DV, drug development
proglumide: DV, drug development
spiradoline: DV, drug development
superfit: DV, drug development
tifluadom: DV, drug development
unindexed drug
uphit: DV, drug development
unclassified drug

RN (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (3,4 dichloro n methyl n [1 phenyl 2 (1 pyrrolidinyl)ethyl]benzeneacetamide) 115199-84-3; (8 [(3,4 dichlorophenyl)acetyl] 7 (1 pyrrolidinylmethyl) 1,4 dioxa 8 azaspiro[4.5]decane) 125104-16-7; (asperlicin) 93413-04-8; (benzotript) 39544-74-6; (beta funaltrexamine) 72782-05-9; (butorphanol) 42408-82-2; (devazepide) **103420-77-5**; (ethylketazocine) 36292-66-7; (fentanyl) 437-38-7; (lorglumide) 97964-56-2; (loxiglumide) 107097-80-3; (meptazinol) 54340-58-8; (morphine) 52-26-6, 57-27-2; (n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzo[b]thiophene 4 acetamide) 111728-01-9; (n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide) 96744-75-1; (naloxone) 357-08-4, 465-65-6; (naltrindole) 111555-53-4; (norbinaltorphimine) 105618-26-6; (pethidine) 28097-96-3, 50-13-5, 57-42-1; (proglumide) 6620-60-6; (spiradoline) 87151-85-7; (tifluadom) 83386-35-0
CN U 69593; U 62066; Ici 199441; Pd 117302; Gr 45809

L29 ANSWER 109 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 92181662 EMBASE
DOCUMENT NUMBER: 1992181662
TITLE: Cholecystokinin administered intrathecally selectively

antagonizes intracerebroventricular β-endorphin-induced tail-flick inhibition in the mouse.

AUTHOR: Tseng L.F.; Collins K.A.
CORPORATE SOURCE: Dept. of Pharmacology and Toxicology, Medical College of Wisconsin, P.O. Box 26509,Milwaukee, WI 53226, United States

SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1992) Vol. 260, No. 3, pp. 1086-1092.
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 920719
Last Updated on STN: 920719

AB The effects of sulfated cholecystokinin octapeptide (CCK8s) given intrathecally (i.t.) or intracerebroventricularly (i.c.v.) on inhibition of the tail-flick and paw-licking hot-plate responses induced by β-endorphin, morphine, D-Ala2-N-Me-Phe4-Gly-ol-Enkephalin (DAMGO) and D-Pen2-D-Pen5- Enkephalin (DPDPE), given i.t. or i.c.v., were studied in male ICR mice. CCK8s (1 ng) given i.t. effectively antagonized inhibition of the tail-flick response induced by i.c.v. administered β-endorphin (2 μg) and DPDPE (10 μg) but not morphine (4 μg) or DAMGO (0.02 μg). However, CCK8s given i.t. did not affect inhibition of the hot-plate response induced by any of the opioid agonists. CCK8s (0.2-40 ng) in combination with β-endorphin (2 μg) or morphine (4 μg) given i.c.v. did not affect β-endorphin- or morphine- induced inhibition of the tail-flick and hot-plate responses. CCK8s and its fragments given i.t. attenuated i.c.v. β-endorphin-induced tail-flick inhibition with different potencies and efficacies. CCK8s was the most potent compound in antagonizing i.c.v. β-endorphin-induced tail-flick inhibition. The rank order of potencies was CCK8s > CCK(27-33) >> caerulein. All three compounds were efficacious, whereas CCK(30-33) was not, in antagonizing β- endorphin-induced tail-flick inhibition. Intrathecal administration of CCK8s (1 ng) significantly attenuated the tail-flick inhibition induced by i.t. β- endorphin (0.5-1 μg) and DPDPE (5 μg) but not morphine (0.5-1 μg), DAMGO (5 ng), norepinephrine (5 ng) or serotonin (16 μg). The inhibition of the hot-plate response induced by i.t. administration of these agonists was not affected by i.t. CCK8s. The inhibitory effect of CCK8s given i.t. on i.c.v. β-endorphin-induced tail-flick inhibition is mediated by stimulation of cholecystokinin receptors, because the respective cholecystokinin A and B receptor blockers L364,718 (0.25-15 pg) and L365,260 (3-100 pg), given i.t., dose-dependently antagonized the effect caused by CCK8s. It is concluded that CCK8s given i.t. selectively attenuates i.c.v. β-endorphin-induced inhibition of the tail-flick response by inhibiting descending ε-opioid system activated by supraspinally applied β-endorphin.

CT Medical Descriptors:
*antinociception
*tail flick test
animal experiment
conference paper
drug antagonism
drug efficacy
drug potency

hot plate test
intracerebroventricular drug administration
intrathecal drug administration
licking
male
mouse
nonhuman
priority journal
Drug Descriptors:
cholecystokinin receptor
epsilon opiate receptor
mu opiate receptor
sigma opiate receptor
*beta endorphin: AD, drug administration
*beta endorphin: CB, drug combination
*beta endorphin: IT, drug interaction
*cholecystokinin octapeptide: AD, drug administration
*cholecystokinin octapeptide: CB, drug combination
*cholecystokinin octapeptide: CM, drug comparison
*cholecystokinin octapeptide: IT, drug interaction
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: IT, drug interaction
3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzamide: IT, drug interaction
3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate
ceruletide: CM, drug comparison
ceruletide: IT, drug interaction
ceruletide: AD, drug administration
cholecystokinin derivative: AD, drug administration
cholecystokinin derivative: CM, drug comparison
cholecystokinin derivative: IT, drug interaction
cholecystokinin receptor blocking agent: IT, drug interaction
devazepide: IT, drug interaction
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: IT, drug interaction
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: AD, drug administration
enkephalin[2,5 dextro penicillamine]: IT, drug interaction
enkephalin[2,5 dextro penicillamine]: AD, drug administration
morphine: CB, drug combination
morphine: AD, drug administration
morphine: IT, drug interaction
noradrenalin: IT, drug interaction
opiate agonist: IT, drug interaction
serotonin: IT, drug interaction
tetragastrin: IT, drug interaction
tetragastrin: CM, drug comparison
tetragastrin: AD, drug administration

RN (beta endorphin) 59887-17-1; (cholecystokinin octapeptide) 25126-32-3; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzamide) 112465-94-8; (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate) 83913-06-8; (ceruletide) 17650-98-5; (devazepide) **103420-77-5**; (enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]) 78123-71-4; (enkephalin[2,5 dextro penicillamine]) 88373-73-3, 88381-29-7; (morphine) 52-26-6, 57-27-2; (noradrenalin) 1407-84-7, 51-41-2; (serotonin) 50-67-9; (tetragastrin) 1947-37-1

CN (1) L 365260; (2) L 364718; (3) U 50488h
CO (2) Merck sharp and dohme (United States); (3) Research biochemicals (United States); Peninsula (United States); Bachem (United States); Aldrich (United States); Sigma (United States); Mallinckrodt (United States)

L29 ANSWER 110 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 92171466 EMBASE
DOCUMENT NUMBER: 1992171466
TITLE: Cholecystokinin antianalgesia: Safety cues abolish morphine analgesia.
AUTHOR: Wiertelak E.P.; Maier S.F.; Watkins L.R.
CORPORATE SOURCE: Department of Psychology, University of Colorado,Boulder, CO 80309, United States
SOURCE: Science, (1992) Vol. 256, No. 5058, pp. 830-833.
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 920705
Last Updated on STN: 920705

AB Environmental stimuli that signal the occurrence of aversive or dangerous events activate endogenous opiate analgesia systems. Signals for safety (the nonoccurrence of aversive events) produce the opposite and inhibit environmentally produced analgesia. Stimuli that signal safety are now shown to abolish the analgesic effect of morphine, even when morphine is applied directly to spinal cord. Further, this antiopiate effect occurs because the environmental stimulus leads to release of the neuropeptide cholecystokinin in the spinal cord. This process may contribute to the regulation of pain and the development of opiate tolerance.

CT Medical Descriptors:
*analgesia
*hazard
*pain: DT, drug therapy
*safety
*signal transduction
*spinal cord
animal experiment
article
controlled study
intrathecal drug administration
nonhuman
priority journal
rat
Drug Descriptors:
*1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
*1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: DO, drug dose
*1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CM, drug comparison
*1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CB, drug combination

*cholecystokinin: EC, endogenous compound
***morphine: PD, pharmacology**
***morphine: DT, drug therapy**
***morphine: CB, drug combination**
***opiate: PD, pharmacology**
***opiate: DT, drug therapy**
devazepide: PD, pharmacology
devazepide: CM, drug comparison
devazepide: CB, drug combination
RN (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (cholecystokinin) 9011-97-6, 93443-27-7; (morphine) 52-26-6, 57-27-2; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (devazepide) **103420-77-5**
CN Mk 329; L 365260

L29 ANSWER 111 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 93025883 EMBASE
DOCUMENT NUMBER: 1993025883
TITLE: Mechanisms of neurotensin effects on pancreatic and duodenal bicarbonate secretion in the rat.
AUTHOR: Nagain C.; Merlin D.; Chariot J.; Roze C.
CORPORATE SOURCE: INSERM U239 Faculte X. Bichat, 16 rue H. Huchard,75018 Paris, France
SOURCE: Annals of the New York Academy of Sciences, (1992) Vol. 668, pp. 359-360.
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 930221
Last Updated on STN: 930221
CT Medical Descriptors:
*duodenum secretion
*pancreas secretion
animal experiment
conference paper
gastrointestinal motility
intravenous drug administration
male
nonhuman
priority journal
rat
stomach secretion
subcutaneous drug administration
Drug Descriptors:
*bicarbonate: EC, endogenous compound
*neurotensin: DO, drug dose
*neurotensin: PD, pharmacology
*neurotensin: IT, drug interaction
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: DO, drug dose
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: IT, drug interaction

atropine: DO, drug dose
atropine: IT, drug interaction
atropine: PD, pharmacology
cholecystokinin receptor blocking agent: DO, drug dose
cholecystokinin receptor blocking agent: IT, drug interaction
cholecystokinin receptor blocking agent: PD, pharmacology
devazepide: PD, pharmacology
devazepide: IT, drug interaction
devazepide: DO, drug dose
hexamethonium bromide: IT, drug interaction
hexamethonium bromide: PD, pharmacology
hexamethonium bromide: DO, drug dose
idazoxan: IT, drug interaction
idazoxan: PD, pharmacology
idazoxan: DO, drug dose
idazoxan: CB, drug combination
indometacin: PD, pharmacology
indometacin: DO, drug dose
indometacin: IT, drug interaction
methadone: DO, drug dose
methadone: IT, drug interaction
methadone: PD, pharmacology
naloxone: PD, pharmacology
naloxone: IT, drug interaction
naloxone: DO, drug dose
prazosin: PD, pharmacology
prazosin: IT, drug interaction
prazosin: DO, drug dose
prazosin: CB, drug combination
propranolol: PD, pharmacology
propranolol: IT, drug interaction
propranolol: DO, drug dose
propranolol: CB, drug combination

RN (bicarbonate) 144-55-8, 71-52-3; (neurotensin) 39379-15-2; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (atropine) 51-55-8, 55-48-1; (devazepide) **103420-77-5** ; (hexamethonium bromide) 55-97-0; (idazoxan) 79944-56-2, 79944-58-4; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (methadone) 1095-90-5, 125-56-4, 23142-53-2, 297-88-1, 76-99-3; (naloxone) 357-08-4, 465-65-6; (prazosin) 19216-56-9, 19237-84-4; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6

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ACCESSION NUMBER: 92104144 EMBASE
DOCUMENT NUMBER: 1992104144
TITLE: Neuropeptides. Function and clinical applications.
AUTHOR: Hughes J.; Woodruff G.N.
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Hills Road, Cambridge, CB2 2QB, United Kingdom
SOURCE: Arzneimittel-Forschung/Drug Research, (1992) Vol. 42, No. 2 A, pp. 250-255.
ISSN: 0004-4172 CODEN: ARZNAD
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
032 Psychiatry
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 920508
Last Updated on STN: 920508

AB Neuropeptides are the most abundant chemical messengers in the brain and their major role seems to be the modulation of amine and amino acid neurotransmission. This appears to be achieved at many sites by the co-release of peptide with the primary transmitter. The presynaptic biochemistry and physiology of neuropeptides ensure that neuromodulation is highly plastic with almost infinite adaptive potential. The recent development of novel drugs (termed peptoids) that mimic or block neuropeptide function have opened up new clinical approaches to a number of conditions. Thus high efficacy kappa opioid-receptor agonists such as CI-977 (enadoline) have potential for the treatment of pain and stroke whilst the development of highly selective and bioavailable cholecystokinin B (CCK-B) antagonists such as CI-988([R-(R*,R*)]-4-[[2 [[3-(1H-indol- 3-yl)-2-methyl-1-ox6-2-[[tricyclo[3.3.1.1.3.1]dec-2-yloxy)carbonyl]amino]propyl]amino]-1-phenethyl]amino-4-oxobutanoic acid) have offered new insights into the mechanisms underlying and the treatment of anxiety disorders and drug abuse. In general it appears that peptoids may offer a greater selectivity of drug action when compared to amino acid/amine based compounds. Peptoid antagonists appear to be relatively free of side effects possibly because neuropeptide systems are only activated under very selective conditions. Peptoid agonists on the other hand can exert extremely powerful actions on brain function and this may be related to the key position neuropeptide receptors occupy in the hierarchy of chemical communication in the brain.

CT Medical Descriptors:
*brain
*neurotransmission
animal tissue
anxiety
conference paper
drug abuse
mouse
pain
priority journal
rat
withdrawal syndrome
Drug Descriptors:
*4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: PD, pharmacology
*4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine: CM, drug comparison
*cholecystokinin receptor blocking agent: PD, pharmacology
*cholecystokinin receptor blocking agent: CM, drug comparison
***enadoline: CM, drug comparison**
***enadoline: PD, pharmacology**
*neuropeptide: EC, endogenous compound
*opiate receptor affecting agent: CM, drug comparison
*opiate receptor affecting agent: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CM, drug comparison
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
cholecystokinin derivative: PD, pharmacology
cholecystokinin derivative: CM, drug comparison

devazepide: PD, pharmacology
devazepide: CM, drug comparison
lorglumide: CM, drug comparison
lorglumide: PD, pharmacology
morphine: PD, pharmacology
morphine: CM, drug comparison
pentagastrin: PD, pharmacology
pentagastrin: CM, drug comparison
pentazocine: PD, pharmacology
pentazocine: CM, drug comparison

RN (4 [[2 [2 [[(2 adamantyloxy)carbonyl]amino] 3 (1h indol 3 yl) 2 methylpropionamido] 1 phenylethyl]amino] 4 oxobutyric acid meglumine) 130404-91-0; (enadoline) 107431-28-7; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (devazepide) **103420-77-5**; (lorglumide) 97964-56-2; (morphine) 52-26-6, 57-27-2; (pentagastrin) 5534-95-2; (pentazocine) 359-83-1, 64024-15-3

CN Ci 977; Ci 988; L 364718; L 365260; Cr 1409

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ACCESSION NUMBER: 92302017 EMBASE
DOCUMENT NUMBER: 1992302017
TITLE: Pentazocine reduces cholinergic responses in the guinea-pig, extrahepatic biliary tract by a non-opiate mechanism.
AUTHOR: Vromen A.; Hanani M.
CORPORATE SOURCE: Laboratory of Experimental Surgery, Hadassah University Hospital, Mount Scopus,Jerusalem 91240, Israel
SOURCE: Journal of Basic and Clinical Physiology and Pharmacology, (1992) Vol. 3, No. 1, pp. 71-79.
ISSN: 0334-1534 CODEN: JBPPES
COUNTRY: Israel
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 921108
Last Updated on STN: 921108

CT Medical Descriptors:
*common bile duct
*gallbladder
*smooth muscle contractility
animal tissue
article
cholinergic system
concentration response
controlled study
drug antagonism
electrostimulation
guinea pig
male
nonhuman
Drug Descriptors:
*carbachol: PD, pharmacology
*carbachol: IT, drug interaction
***pentazocine: IT, drug interaction**

***pentazocine: PD, pharmacology**
atropine: PD, pharmacology
chlorpheniramine: PD, pharmacology
cholecystokinin octapeptide: PD, pharmacology
cholecystokinin receptor blocking agent: PD, pharmacology
devazepide: PD, pharmacology
haloperidol: PD, pharmacology
histamine: PD, pharmacology
indometacin: PD, pharmacology
naloxone: PD, pharmacology
phentolamine: PD, pharmacology
phenylephrine: PD, pharmacology
propranolol: PD, pharmacology
tetrodotoxin: TO, drug toxicity
RN (carbachol) 462-58-8, 51-83-2; (pentazocine) 359-83-1, 64024-15-3; (atropine) 51-55-8, 55-48-1; (chlorpheniramine) 132-22-9; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5**; (haloperidol) 52-86-8; (histamine) 51-45-6, 56-92-8, 93443-21-1; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (naloxone) 357-08-4, 465-65-6; (phentolamine) 50-60-2, 73-05-2; (phenylephrine) 532-38-7, 59-42-7, 61-76-7; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (tetrodotoxin) 4368-28-9, 4664-41-9
CN (1) L 364718
CO (1) Merck sharp and dohme; Du pont; Schering; Winthrop breon laboratories; Ciba geigy; Sigma

L29 ANSWER 114 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 91322001 EMBASE
DOCUMENT NUMBER: 1991322001
TITLE: Lorglumide.
SOURCE: Drugs of the Future, (1991) Vol. 16, No. 9, pp. 865-866.
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 920305
Last Updated on STN: 920305
CT Medical Descriptors:
*drug antagonism
*pancreatitis
*smooth muscle contraction
*stomach acid secretion
animal experiment
animal tissue
guinea pig
human
human tissue
intestine
intraperitoneal drug administration
intravenous drug administration
nonhuman
opossum
rat
short survey
Drug Descriptors:

*cholecystokinin receptor blocking agent: CB, drug combination
*cholecystokinin receptor blocking agent: CM, drug comparison
*cholecystokinin receptor blocking agent: IT, drug interaction
*cholecystokinin receptor blocking agent: PD, pharmacology
*lorglumide: PD, pharmacology
*lorglumide: CM, drug comparison
*lorglumide: CB, drug combination
*lorglumide: IT, drug interaction
amylase: EC, endogenous compound
cholecystokinin octapeptide: CB, drug combination
cholecystokinin octapeptide: IT, drug interaction
devazepide: CM, drug comparison
loxiglumide: CM, drug comparison
morphine: IT, drug interaction
morphine: CB, drug combination
RN (lorglumide) 97964-56-2; (amylase) 9000-90-2, 9000-92-4, 9001-19-8; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5**; (loxiglumide) 107097-80-3; (morphine) 52-26-6, 57-27-2
CO Tokyo tanabe; Rotta

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ACCESSION NUMBER: 91321990 EMBASE
DOCUMENT NUMBER: 1991321990
TITLE: Devazepide, L-364718, MK-329.
SOURCE: Drugs of the Future, (1991) Vol. 16, No. 9, pp. 853-856.
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 920305
Last Updated on STN: 920305
CT Medical Descriptors:
*behavior
*cytotoxicity
*drug receptor binding
*hunger
*pancreatitis: DT, drug therapy
*smooth muscle relaxation
animal cell
animal experiment
animal tissue
dna synthesis
drug antagonism
guinea pig
human
human experiment
intestine
intracerebroventricular drug administration
intraperitoneal drug administration
male
monkey
mouse
nonhuman
normal human
rabbit

rat
short survey
stomach
subcutaneous drug administration
Drug Descriptors:
*cholecystokinin receptor blocking agent: PD, pharmacology
*cholecystokinin receptor blocking agent: DT, drug therapy
*cholecystokinin receptor blocking agent: IT, drug interaction
*cholecystokinin receptor blocking agent: CB, drug combination
*cholecystokinin receptor blocking agent: CM, drug comparison
*devazepide: DT, drug therapy
*devazepide: PD, pharmacology
*devazepide: CM, drug comparison
*devazepide: CB, drug combination
*devazepide: IT, drug interaction
***morphine: CB, drug combination**
***morphine: IT, drug interaction**
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: DO, drug dose
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea: CM, drug comparison
4 bromo n (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl)benzamide: CM, drug comparison
4 bromo n (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl)benzamide: PD, pharmacology
amylase: EC, endogenous compound
cholecystokinin octapeptide: PD, pharmacology
cholecystokinin octapeptide: IT, drug interaction
cholecystokinin octapeptide: CB, drug combination
cholecystokinin octapeptide: CM, drug comparison
diazepam: CM, drug comparison
gastrin: CM, drug comparison
gastrin: PD, pharmacology
lorglumide: CM, drug comparison
loxiglumide: CM, drug comparison
placebo: CM, drug comparison

RN (devazepide) **103420-77-5**; (morphine) 52-26-6, 57-27-2; (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (4 bromo n (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl)benzamide) 111035-59-7; (amylase) 9000-90-2, 9000-92-4, 9001-19-8; (cholecystokinin octapeptide) 25126-32-3; (diazepam) 439-14-5; (gastrin) 9002-76-0; (lorglumide) 97964-56-2; (loxiglumide) 107097-80-3
CN (1) Mk 329; L 364718
CO (1) Merck

L29 ANSWER 116 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 91148070 EMBASE
DOCUMENT NUMBER: 1991148070
TITLE: The partnership of academia and industry in pharmacologic research.
AUTHOR: Scolnick E.M.
CORPORATE SOURCE: Merck Sharp and Dohme, Research Laboratories, P.O. Box 2000,Rahway, NJ 07065, United States
SOURCE: Journal of Laboratory and Clinical Medicine, (1991) Vol. 117, No. 1, pp. 8-14.

ISSN: 0022-2143 CODEN: JLCMAK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911216
Last Updated on STN: 911216
CT Medical Descriptors:
*drug research
*industry
*pharmacology
article
priority journal
Drug Descriptors:
*acetylsalicylic acid: DV, drug development
*aciclovir: DV, drug development
*beta lactam antibiotic: DV, drug development
*captopril: DV, drug development
*digitalis: DV, drug development
*methotrexate: DV, drug development
losartan potassium: DV, drug development
androgen: DV, drug development
benzodiazepine derivative: DV, drug development
colony stimulating factor: DV, drug development
corticosteroid: DV, drug development
cyclosporin: DV, drug development
devazepide: DV, drug development
diltiazem: DV, drug development
erythropoietin: DV, drug development
estrogen: DV, drug development
fluconazole: DV, drug development
growth hormone: DV, drug development
insulin: DV, drug development
itraconazole: DV, drug development
ketoconazole: DV, drug development
mevinolin: DV, drug development
morphine: DV, drug development
nifedipine: DV, drug development
omeprazole: DV, drug development
procainamide: DV, drug development
quinidine: DV, drug development
quinoline derivative: DV, drug development
tissue plasminogen activator: DV, drug development
vaccine: DV, drug development
verapamil: DV, drug development
RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (aciclovir) 59277-89-3; (captopril) 62571-86-2; (digitalis) 8031-42-3, 8053-83-6; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (losartan potassium) 124750-99-8; (colony stimulating factor) 62683-29-8; (cyclosporin) 79217-60-0; (devazepide) **103420-77-5**; (diltiazem) 33286-22-5, 42399-41-7; (erythropoietin) 11096-26-7; (fluconazole) 86386-73-4; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (insulin) 9004-10-8; (itraconazole) 84625-61-6; (ketoconazole) 65277-42-1; (mevinolin) 75330-75-5; (morphine) 52-26-6, 57-27-2; (nifedipine) 21829-25-4; (omeprazole) 73590-58-6, 95510-70-6; (procainamide) 51-06-9, 614-39-1; (quinidine) 56-54-2; (tissue plasminogen activator) 105913-11-9; (verapamil) 152-11-4, 52-53-9

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ACCESSION NUMBER: 90264409 EMBASE
DOCUMENT NUMBER: 1990264409
TITLE: Behavioral effects of cholecystokinin mediated by CCK-A receptors in rat and mouse brain.
AUTHOR: Ott T.; Fink H.; Gericke M.
CORPORATE SOURCE: Institut of Pharmacology and Toxicology, Humboldt-University, PF 140, 1040 Berlin, Germany
SOURCE: European Journal of Pharmacology, (1990) Vol. 183, No. 3, pp. 1120.
ISSN: 0014-2999 CODEN: EJPHAZ
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911213
Last Updated on STN: 911213
CT Medical Descriptors:
*analgesia
*behavior
*locomotion
mouse
rat
psychological aspect
animal experiment
nonhuman
intracerebral drug administration
intracerebroventricular drug administration
conference paper
priority journal
Drug Descriptors:
*cholecystokinin receptor
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: PD, pharmacology
*cholecystokinin octapeptide: PD, pharmacology
*devazepide: PD, pharmacology
*quinpirole: PD, pharmacology
***tifluadom: PD, pharmacology**
RN (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5** ; (quinpirole) 73625-62-4, 80373-22-4, 85760-75-4, 85798-08-9; (tifluadom) 83386-35-0
CN Skf 38393; Ly 171555; Mk 329

L29 ANSWER 118 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 90038573 EMBASE
DOCUMENT NUMBER: 1990038573
TITLE: Cholecystokinin-A receptor ligands based on the κ-opioid agonist tifluadom.
AUTHOR: Bock M.G.; DiPardo R.M.; Evans B.E.; Rittle K.E.; Whitter W.L.; Veber D.F.; Freidinger R.M.; Chang R.S.L.; Chen T.B.; Lotti V.J.
CORPORATE SOURCE: Department of Medicinal Chemistry and Microbial Pharmacometrics, Merck Sharp and Dohme Research

Laboratories, West Point, PA 19486, United States
SOURCE: Journal of Medicinal Chemistry, (1990) Vol. 33, No. 1, pp. 450-455.
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911213
Last Updated on STN: 911213

AB Tifluadom, a κ-opioid agonist and cholecystokinin-A (CCK-A) receptor antagonist, was utilized as a model to prepare a series of 2-(aminomethyl)- and 3-(aminomethyl)-1,4-benzodiazepines. These compounds were tested in vitro as inhibitors of the binding of [125I]CCK to rat pancreas and guinea pig brain receptors. All compounds with IC50's less than 100 μM proved to have greater affinity for the CCK-A receptor, with the most potent analogue, 6e, having an IC50 of 0.16 μM. The benzodiazepines described in this study are simultaneously CCK-A and opioid receptor ligands. The ramification of this dichotomy on current concepts of peptide hormone action are discussed. These results further demonstrate the versatility of the benzodiazepine core structure for designing nonpeptide ligands for peptide receptors and the ability to fine-tune the receptor interactions of these benzodiazepines by appropriate structure modifications.

CT Medical Descriptors:
*drug receptor binding
*drug screening
*drug synthesis
brain
guinea pig
rat
animal cell
nonhuman
article
priority journal
Drug Descriptors:
*opiate receptor
cholecystokinin a receptor
*benzodiazepine derivative: PD, pharmacology
*benzodiazepine derivative: CM, drug comparison
*benzodiazepine derivative: AN, drug analysis
*benzodiazepine derivative: DV, drug development
cholecystokinin octapeptide
dihydromorphine
devazepide
n (2,3 dihydro 1 methyl 5 (2 fluorophenyl) 1h 1,4 benzodiazepin 2 ylmethyl) 1h indole 2 carboxamide: PD, pharmacology
n (2,3 dihydro 1 methyl 5 (2 fluorophenyl) 1h 1,4 benzodiazepin 2 ylmethyl) 1h indole 2 carboxamide: CM, drug comparison
n (2,3 dihydro 1 methyl 5 (2 fluorophenyl) 1h 1,4 benzodiazepin 2 ylmethyl) 1h indole 2 carboxamide: AN, drug analysis
n (2,3 dihydro 1 methyl 5 (2 fluorophenyl) 1h 1,4 benzodiazepin 2 ylmethyl) 1h indole 2 carboxamide: DV, drug development
naloxone
unclassified drug

RN (cholecystokinin octapeptide) 25126-32-3; (dihydromorphine) 1421-28-9, 509-60-4; (devazepide) **103420-77-5**; (naloxone) 357-08-4,

465-65-6
CN L 364718

L29 ANSWER 119 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 91072090 EMBASE
DOCUMENT NUMBER: 1991072090
TITLE: Influences of cholecystokinin and analogues on memory processes.
AUTHOR: Itoh S.; Lal H.
CORPORATE SOURCE: Department of Pharmacology, Texas College of Osteopathic, Medicine, 3500 Camp Bowie,Fort Worth, TX 76107, United States
SOURCE: Drug Development Research, (1990) Vol. 21, No. 4, pp. 257-276.
ISSN: 0272-4391 CODEN: DDREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911216
Last Updated on STN: 911216

AB Evidence is reviewed to assign the role of cholecystokinins in the cognitive and memory processes. Rat brain contains about 550 ng of CCK-8. When injected, icv or sc, in doses of less than 100 ng of CCK or caerulein, these peptides prevent experimental amnesia and prolong extinction of the already-learned tasks. Caerulein is nearly 10 times as potent as CCK-8, and the effects of both peptides are long-lasting. Pretreatment with these peptides also prevents scopolamine-induced amnesia, and reverses the ACh depletion in the frontal and temporal cortices as well as in the hippocampus. CCK-8 antagonists in small doses produce complete amnesia, further supporting the hypothesis that endogenous CCK-8 modulates the memory processes in the brain. Neurochemical data suggest participation of the NMDA receptors, protein kinase C, and protein synthesis in the action of CCK-8 and caerulein. Sub-diaphragmatical vagotomy abolishes the memory-enhancing effects of these peptides when administered peripherally. Thus, CCK-8 and caerulein are likely to affect not only the receptors localized in the CNS, but also to stimulate peripheral receptors associated with the vagus. Alternatively, the vagus may be the major pathway for CCK transport from the visceral organs to the brain.

CT Medical Descriptors:
*amnesia
*behavior
*memory
animal experiment
appetite
cholinergic system
human
human experiment
intracerebroventricular drug administration
intramuscular drug administration
intraperitoneal drug administration
nonhuman
priority journal
protein synthesis

rat
review
schizophrenia
subcutaneous drug administration
vagotomy
Drug Descriptors:
n methyl dextro aspartic acid receptor
*ceruletide: CM, drug comparison
*ceruletide: PD, pharmacology
*cholecystokinin octapeptide: DO, drug dose
*cholecystokinin octapeptide: IT, drug interaction
*cholecystokinin octapeptide: CM, drug comparison
*cholecystokinin octapeptide: CB, drug combination
*cholecystokinin octapeptide: EC, endogenous compound
*cholecystokinin octapeptide: PD, pharmacology
*devazepide: CB, drug combination
*devazepide: PD, pharmacology
*devazepide: IT, drug interaction
*proglumide: PD, pharmacology
*proglumide: IT, drug interaction
*proglumide: CB, drug combination
*tetragastrin: PD, pharmacology
*tetragastrin: IT, drug interaction
*tetragastrin: CM, drug comparison
*tetragastrin: CB, drug combination
*valylprolylvalylglutamylalanylvalylaspartylprolylmethionine: PD, pharmacology
*valylprolylvalylglutamylalanylvalylaspartylprolylmethionine: CM, drug comparison
2 amino 5 phosphonovaleric acid: CB, drug combination
2 amino 5 phosphonovaleric acid: PD, pharmacology
2 amino 5 phosphonovaleric acid: IT, drug interaction
2 amino 5 phosphonovaleric acid: CM, drug comparison
2 amino 7 phosphonoheptanoic acid: CB, drug combination
2 amino 7 phosphonoheptanoic acid: CM, drug comparison
2 amino 7 phosphonoheptanoic acid: IT, drug interaction
2 amino 7 phosphonoheptanoic acid: PD, pharmacology
acetylcholine: EC, endogenous compound
beta endorphin: CB, drug combination
beta endorphin: PD, pharmacology
beta endorphin: IT, drug interaction
dizocilpine: CB, drug combination
dizocilpine: PD, pharmacology
dizocilpine: IT, drug interaction
naloxone: PD, pharmacology
naloxone: IT, drug interaction
naloxone: CB, drug combination
phencyclidine: PD, pharmacology
phencyclidine: IT, drug interaction
phencyclidine: CM, drug comparison
phencyclidine: CB, drug combination
phencyclidine: TO, drug toxicity
protein kinase c: EC, endogenous compound
scopolamine: PD, pharmacology
serotonin: EC, endogenous compound
vasopressin: EC, endogenous compound
RN (ceruletide) 17650-98-5; (cholecystokinin octapeptide) 25126-32-3; (devazepide) **103420-77-5**; (proglumide) 6620-60-6; (tetragastrin) 1947-37-1; (valylprolylvalylglutamylalanylvalylaspartylprolylmethionine)

99291-20-0; (2 amino 5 phosphonovaleric acid) 76726-92-6; (2 amino 7 phosphonoheptanoic acid) 85797-13-3; (acetylcholine) 51-84-3, 60-31-1, 66-23-9; (beta endorphin) 59887-17-1; (dizocilpine) 77086-21-6; (naloxone) 357-08-4, 465-65-6; (phencyclidine) 77-10-1, 956-90-1; (protein kinase c) 141436-78-4; (scopolamine) 138-12-5, 51-34-3, 55-16-3; (serotonin) 50-67-9; (vasopressin) 11000-17-2

L29 ANSWER 120 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 89206310 EMBASE
DOCUMENT NUMBER: 1989206310
TITLE: Influence of L-364,718, a specific CCK-A antagonist, on pain threshold, morphine analgesia and opioid receptors.
AUTHOR: Marrama D.; Poggioli R.; Vergoni A.V.; Sandrini M.; Bertolini A.
CORPORATE SOURCE: Institute of Pharmacology, University of Modena, 41100 Modena, Italy
SOURCE: Pharmacological Research, (1989) Vol. 21, No. 4, pp. 473-474.
ISSN: 0031-6989 CODEN: PHMREP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212
CT Medical Descriptors:
*analgesia
mouse
pain threshold
abstract report
animal experiment
nonhuman
intracerebroventricular drug administration
intraperitoneal drug administration
Drug Descriptors:
*cholecystokinin receptor blocking agent
*opiate receptor
***morphine: PD, pharmacology**
*devazepide: PD, pharmacology
*devazepide: DO, drug dose
RN (morphine) 52-26-6, 57-27-2; (devazepide) **103420-77-5**
CN L 364,718

L29 ANSWER 121 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 90029370 EMBASE
DOCUMENT NUMBER: 1990029370
TITLE: The role of CCK, caerulein, and CCK antagonists in nociception.
AUTHOR: Baber N.S.; Dourish C.T.; Hill D.R.
CORPORATE SOURCE: Merck, Sharp and Dohme Research Laboratories, Eastwick Road, Harlow CM20 2QR, United Kingdom
SOURCE: Pain, (1989) Vol. 39, No. 3, pp. 307-328.
ISSN: 0304-3959 CODEN: PAINDB
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology

024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911213
Last Updated on STN: 911213

AB The octapeptide form of CCK predominates in the central nervous system (CNS) of mammalian species, including man. Many of the physiological roles of CCK in the CNS are unknown, but it is believed to be involved in nociception. CCK is distributed throughout cortical grey matter, periaqueductal grey matter, ventromedial thalamus and spinal dorsal horn, all of which are areas known to be associated with pain modulation. CCK receptor subtypes have been identified and may be classified according to their affinity for the sulphated and desulphated forms of CCK-8 and the recently described selective antagonist, MK-329. CCK-A receptors have high affinity for sulphated CCK-8 and for MK-329 but low affinity for desulphated CCK-8 and CCK-4 whilst CCK-B sites bind MK-329 with low affinity and discriminate poorly between sulphated and desulphated CCK-8. CCK-A receptors are found predominantly in peripheral tissues but they also exist in discrete regions of the primate CNS, including the spinal cord. CCK-B receptors are found ubiquitously throughout other regions of the neuraxis. The results of studies on the effects of CCK-8 and the decapeptide analogue caerulein on pain thresholds are conflicting. Some workers suggest that large doses of CCK-8 and caerulein induce naloxone-reversible analgesia in certain pain models. However, it appears likely that analgesia induced by large doses of CCK and caerulein in animals may be a pharmacological rather than a physiological phenomenon. Accordingly others have found that small (and most probably, physiological) doses of CCK-8 attenuate the analgesic effects of morphine, and of endogenous opioids. Thus, it has been proposed that CCK may act as an endogenous opiate antagonist. Studies in rats with the selective CCK antagonist MK-329 have helped clarify the interaction between CCK and morphine-induced analgesia. Treatment with MK-329 enhances morphine analgesia and chronic treatment with MK-329 prevents the development of tolerance to morphine analgesia. However, the antagonist does not prevent naloxone-precipitated withdrawal symptoms in morphine-dependent rats. In man, caerulein prevents pain associated with gall-bladder contraction, probably by relaxation of the sphincter of Oddi. Caerulein has also been shown to reduce renal colic and the pain of intermittent claudication. Preliminary clinical studies with the weak, non-selective, CCK antagonist proglumide, indicate an enhancement of morphine analgesia. As yet, no studies have demonstrated analgesic effects of CCK antagonists in man when administered alone. It is possible that selective and specific CCK antagonists may have a therapeutic role in enhancing exogenous and endogenous opioid analgesia and in preventing tolerance to opioid analgesics.

CT Medical Descriptors:
*central nervous system
*nociception
pain
rat
animal experiment
nonhuman
intracerebral drug administration
intraperitoneal drug administration
intrathecal drug administration
subcutaneous drug administration
article
priority journal

Drug Descriptors:
neurotransmitter
*ceruletide: PD, pharmacology
*cholecystokinin octapeptide: AD, drug administration
*cholecystokinin octapeptide: CB, drug combination
*cholecystokinin octapeptide: IT, drug interaction
*cholecystokinin octapeptide: DO, drug dose
*cholecystokinin octapeptide: PD, pharmacology
***morphine: PD, pharmacology**
***morphine: IT, drug interaction**
***morphine: CB, drug combination**
*devazepide: IT, drug interaction
*devazepide: PD, pharmacology
*devazepide: CB, drug combination
***opiate: CB, drug combination**
***opiate: IT, drug interaction**
***opiate: PD, pharmacology**
*proglumide: PD, pharmacology
naloxone
RN (ceruletide) 17650-98-5; (cholecystokinin octapeptide) 25126-32-3; (morphine) 52-26-6, 57-27-2; (devazepide) **103420-77-5**; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (proglumide) 6620-60-6; (naloxone) 357-08-4, 465-65-6
CN Mk 329

L29 ANSWER 122 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 89189727 EMBASE
DOCUMENT NUMBER: 1989189727
TITLE: Cholecystokinin and gastrin antagonists.
AUTHOR: Freidinger R.M.
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, West Point, PA 19486, United States
SOURCE: Medicinal Research Reviews, (1989) Vol. 9, No. 3, pp. 271-290.
ISSN: 0198-6325 CODEN: MRREDD
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 003 Endocrinology
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212
CT Medical Descriptors:
anorexia
brain
irritable colon
pancreas
pancreas carcinoma
pancreatitis
stomach
review
human
nonhuman
Drug Descriptors:
*cholecystokinin receptor
*gastrin

*cholecystokinin receptor blocking agent: DV, drug development
*gastrin antagonist: DV, drug development
amino acid derivative
asperlicin
benzodiazepine derivative
benzotript
cholecystokinin
dibutyryl cyclic gmp
gastrin analog
lorglumide
loxiglumide
devazepide
proglumide
tifluadom
unclassified drug
RN (gastrin) 9002-76-0; (asperlicin) 93413-04-8; (benzotript) 39544-74-6; (cholecystokinin) 9011-97-6, 93443-27-7; (dibutyryl cyclic gmp) 32266-35-6; (lorglumide) 97964-56-2; (loxiglumide) 107097-80-3; (devazepide) **103420-77-5**; (proglumide) 6620-60-6; (tifluadom) 83386-35-0
CN Mk 329

L29 ANSWER 123 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 89189789 EMBASE
DOCUMENT NUMBER: 1989189789
TITLE: Non-peptide ligands for peptide receptors.
AUTHOR: Freidinger R.M.
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, West Point, PA 19486, United States
SOURCE: Trends in Pharmacological Sciences, (1989) Vol. 10, No. 7, pp. 270-274.
ISSN: 0165-6147 CODEN: TPHSDY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212
CT Medical Descriptors:
drug design
short survey
nonhuman
animal
Drug Descriptors:
*angiotensin receptor
*cholecystokinin receptor
*ligand
*opiate receptor
benzodiazepine receptor
*opiate peptide: PD, pharmacology
1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea
2 butyl 4 chloro 1 (2 nitrobenzyl) 5 imidazoleacetic acid
3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate
erythromycin

gonadorelin derivative
ketoconazole
lorglumide
morphine
devazepide
naloxone
naltrindole
norbinaltorphimine
somatostatin analog
tifluadom

RN (1 (2,3 dihydro 1 methyl 2 oxo 5 phenyl 1h 1,4 benzodiazepin 3 yl) 3 (3 methylphenyl)urea) 118101-09-0; (2 butyl 4 chloro 1 (2 nitrobenzyl) 5 imidazoleacetic acid) 119256-78-9; (3,4 dichloro n methyl n [2 (1 pyrrolidinyl)cyclohexyl]benzeneacetamide methanesulfonate) 83913-06-8; (erythromycin) 114-07-8, 70536-18-4; (ketoconazole) 65277-42-1; (lorglumide) 97964-56-2; (morphine) 52-26-6, 57-27-2; (devazepide) **103420-77-5**; (naloxone) 357-08-4, 465-65-6; (naltrindole) 111555-53-4; (norbinaltorphimine) 105618-26-6; (tifluadom) 83386-35-0

CN U 50488 h; Mk 329; L 365260; S 8308

L29 ANSWER 124 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

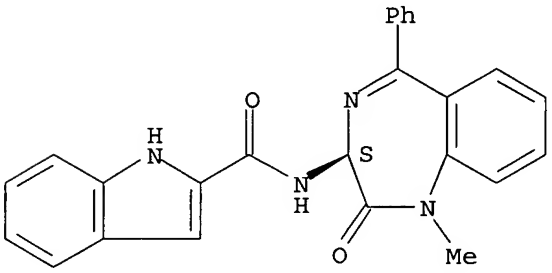
ACCESSION NUMBER: 89285636 EMBASE
DOCUMENT NUMBER: 1989285636
TITLE: Cholecystokinin peptides and bombesin reverse hemorrhagic shock in rats.
AUTHOR: Guarini S.; Tagliavini S.; Bazzani C.; Vergoni A.V.; Bertolini A.
CORPORATE SOURCE: Institute of Pharmacology, University of Modena, Via G. Campi 287, 41100 Modena, Italy
SOURCE: Resuscitation, (1989) Vol. 18, No. 2-3, pp. 129-131. ISSN: 0300-9572 CODEN: RSUSBS
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212

CT Medical Descriptors:
*bleeding
*shock: ET, etiology
rat
animal experiment
nonhuman
intravenous drug administration
priority journal
Drug Descriptors:
*bombesin: PD, pharmacology
*bombesin: DO, drug dose
*ceruletide: PD, pharmacology
*ceruletide: DO, drug dose
*cholecystokinin octapeptide: PD, pharmacology
*cholecystokinin octapeptide: DO, drug dose
atropine
morphine
devazepide
prazosin

reserpine
yohimbine
RN (bombesin) 31362-50-2; (ceruletide) 17650-98-5; (cholecystokinin octapeptide) 25126-32-3; (atropine) 51-55-8, 55-48-1; (morphine) 52-26-6, 57-27-2; (devazepide) **103420-77-5**; (prazosin) 19216-56-9, 19237-84-4; (reserpine) 50-55-5, 8001-95-4; (yohimbine) 146-48-5, 65-19-0
CN L 364718

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 103420-77-5 REGISTRY
ED Entered STN: 26 Jul 1986
CN 1H-Indole-2-carboxamide, N-[(3S)-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-1,4-Benzodiazepine, 1H-indole-2-carboxamide deriv.
CN 1H-Indole-2-carboxamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-, (S)-
OTHER NAMES:
CN Devacade
CN **Devazepide**
CN L 364718
CN MK 329
FS STEREOSEARCH
MF C25 H20 N4 O2
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, NIOSHTIC, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

295 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
295 REFERENCES IN FILE CAPLUS (1907 TO DATE)

IT 111035-59-7 118101-09-0, L 365260
RL: BIOL (Biological study)
(morphine **analgesia** and tolerance response to)
IT **103420-77-5**, MK 329
RL: BIOL (Biological study)
(morphine **analgesia** response to)
IT 9011-97-6, Cholecystokinin
RL: BIOL (Biological study)
(receptor for, antagonists of, morphine **analgesia** and tolerance response to)

L29 ANSWER 84 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:51173 HCAPLUS
DOCUMENT NUMBER: 110:51173
TITLE: Blockade of CCK-induced hypophagia and prevention of morphine tolerance by the CCK antagonist L-364,718
AUTHOR(S): Dourish, Colin T.; Coughlan, Josephine; Hawley, Diane; Clark, Michael; Iversen, Susan D.
CORPORATE SOURCE: Neurosci. Res. Cent., Merck Sharp and Dohme Res. Lab., Harlow/Essex, CM20 2QR, UK
SOURCE: Neurology and Neurobiology (1988), 47(Cholecystokinin Antagonists), 307-25
CODEN: NEUND9; ISSN: 0736-4563
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rats, L-364718 (I) produced a small increase in food intake, but reversed the increase in food intake induced by cholecystokinin (CCK), indicating that CCK may have a role in satiety. Also in rats, selective blockade of CCK receptors by I enhanced morphine **analgesia** by enhancing its peak effect and increasing the duration of **analgesia** . I also prevented the development of tolerance to morphine **analgesia** but did not influence the onset of dependence. These findings support the suggestion that CCK may act as an endogenous opiate antagonist and inhibit the behavioral effects of opiates. Also, a CCK receptor antagonist such as I have therapeutic effects, possibly for use with opiate **analgesia**.
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
ST cholecystokinin antagonist hypophagia morphine **analgesia** tolerance; opioid antagonist cholecystokinin; receptor cholecystokinin antagonist L 364718
IT Receptors
RL: BIOL (Biological study)
(for cholecystokinin, antagonists of, L-364718 as, appetite and morphine **analgesia** tolerance response to)
IT **Analgesia**
(from morphine, tolerance to, cholecystokinin antagonist L-364718 effect on)
IT Drug dependence
(on morphine **analgesia**, cholecystokinin antagonist L-364718 effect on)
IT Drug tolerance
(to morphine **analgesia**, cholecystokinin antagonist L-364718 effect on)
IT **57-27-2**, Morphine, biological studies
RL: BIOL (Biological study)
(**analgesia** from, tolerance to, cholecystokinin antagonist L-364718 effect on)
IT **103420-77-5**

For example L-365,260 had the highest partition coefficient, but the lowest brain extraction Plasma protein binding decreased the uptake by the brain but to a lesser extent than that predicted from the unbound drug fraction in vitro, suggesting that drug binding to plasma protein did not limit the transport of drug through the blood-brain barrier. For L-364,718, the extraction ratio and permeability-surface product values were increased markedly in CCl4-induced hepatic injury. Other disease states (uranyl nitrate-induced renal failure and streptozotocin-induced diabetes) had no apparent effect on the uptake of the compds. tested. The effect of disease states on the brain uptake of the drugs appeared to be dependent on the type of disease and the individual drug studied.

CC 1-2 (Pharmacology)

IT 439-14-5, Diazepam 12794-10-4D, Benzodiazepine, derivs. **103420-77-5**, L 364718 118101-09-0, L 365260 122384-14-9, L 663581
RL: BIOL (Biological study)
(uptake of, by brain, disease and protein binding effect on)

L29 ANSWER 83 OF 124 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:172160 HCAPLUS
DOCUMENT NUMBER: 112:172160
TITLE: The selective CCK-B receptor antagonist L-365,260 enhances morphine **analgesia** and prevents morphine tolerance in the rat
AUTHOR(S): Dourish, C. T.; O'Neill, M. F.; Coughlan, J.; Kitchener, S. J.; Hawley, D.; Iversen, S. D.
CORPORATE SOURCE: Neurosci. Res. Cent., Merck Sharp and Dohme Res. Lab., Harlow/Essex, CM20 2QR, UK
SOURCE: European Journal of Pharmacology (1990), 176(1), 35-44
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of the selective cholecystokinin A (CCK-A) antagonist L-365,031 and the selective CCK-B antagonist L-365,260 on morphine **analgesia** and opiate tolerance and dependence in rats were examined L-365,031 and L-365,260 had no effect on baseline pain thresholds in the radiant heat tail flick test but enhanced **analgesia** induced by a submaximal dose of morphine (4 mg/kg). Similarly, L-365,260 did not effect pain thresholds in the paw pressure test but enhanced morphine **analgesia** in this model. Rats injected twice daily for 6 days with incremental doses of morphine became tolerant to the **analgesic** effects of the drug. Twice daily injections of either 8 mg L-365,031/kg of 0.2 mg L-365,260/kg prevented the development of tolerance to morphine **analgesia**. In contrast, L-365,260 had no influence on the development of opiate dependence in these animals, as assessed by naloxone-precipitated withdrawal. The rank order of potency of non-peptide CCK antagonist for enhancing morphine **analgesia** is L-365,260 > MK-329 > L-365,031. This rank order correlates well with the potency of the antagonists in blocking CCK-B receptors in rodents and suggests that CCK/opiate interactions in this species are mediated by CCK-B receptors.

CC 1-11 (Pharmacology)

ST morphine **analgesia** drug tolerance cholecystokinin antagonist

IT **Analgesia**
(from morphine, cholecystokinin receptor antagonist L 365260 effect on)

IT **57-27-2**, Morphine, biological studies
RL: BIOL (Biological study)
(**analgesia** from and tolerance to, cholecystokinin receptor antagonist L 365260 effect on)

RL: BIOL (Biological study)
(hypophagia from cholecystokinin and morphine **analgesia** tolerance prevention by)
IT 9011-97-6, Cholecystokinin
RL: BIOL (Biological study)
(in appetite regulation and morphine **analgesia** and tolerance, receptor antagonist effect on)

L29 ANSWER 85 OF 124 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002099781 EMBASE
TITLE: The biology of the opioid growth factor receptor (OGFr).
AUTHOR: Zagon I.S.; Verderame M.F.; McLaughlin P.J.
CORPORATE SOURCE: I.S. Zagon, Milton S. Hershey Medical Center, Pennsylvania State University, College of Medicine, 500 University Drive, Hershey, PA 17033, United States. isz1@psu.edu
SOURCE: Brain Research Reviews, (2002) Vol. 38, No. 3, pp. 351-376.
Refs: 159
ISSN: 0165-0173 CODEN: BRERD2
PUBLISHER IDENT.: S 0165-0173(01)00160-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020328
Last Updated on STN: 20020328

AB Opioid peptides act as growth factors in neural and non-neural cells and tissues, in addition to serving for neurotransmission/neuromodulation in the nervous system. The native opioid growth factor (OGF), [Met(5)]-enkephalin, is a tonic inhibitory peptide that plays a role in cell proliferation and tissue organization during development, cancer, cellular renewal, wound healing, and angiogenesis. OGF action is mediated by a receptor mechanism. Assays with radiolabeled OGF have detected specific and saturable binding, with a one-site model of kinetics. Subcellular fractionation studies show that the receptor for OGF (OGFr) is an integral membrane protein associated with the nucleus. Using antibodies generated to a binding fragment of OGFr, this receptor has been cloned and sequenced in human, rat, and mouse. OGFr is distinguished by containing a series of imperfect repeats. The molecular and protein structure of OGFr have no resemblance to that of classical opioid receptors, and have no significant homologies to known domains or functional motifs with the exception of a bipartite nuclear localization signal. Immunoelectron microscopy and immunocytochemistry investigations, including co-localization studies, have detected OGFr on the outer nuclear envelope where it interfaces with OGF. The peptide-receptor complex associates with karyopherin, translocates through the nuclear pore, and can be observed in the inner nuclear matrix and at the periphery of heterochromatin of the nucleus. Signal transduction for modulation of DNA activity is dependent on the presence of an appropriate confirmation of peptide and receptor. This report reviews the history of OGF-OGFr, examines emerging insights into the mechanisms of action of opioid peptide-receptor interfacing, and discusses the clinical significance of these observations. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

CT Medical Descriptors:
cell proliferation

assay
cell fractionation
protein structure
sequence homology
protein domain
protein motif
immunoelectron microscopy
immunocytochemistry
protein localization
heterochromatin
signal transduction
receptor binding
DNA synthesis
drug activity
drug effect
drug potency
angiogenesis
wound healing
drug mechanism
binding site
cancer incidence
molecular biology
gene location
human
nonhuman
review
nucleotide sequence
priority journal
Drug Descriptors:
*growth factor receptor: EC, endogenous compound
*opioid growth factor receptor: EC, endogenous compound
karyopherin
metenkephalin: CM, drug comparison
metenkephalin: PD, pharmacology
leucine enkephalin: PD, pharmacology
beta funaltrexamine: PD, pharmacology
enkephalin[2 dextro alanine 5 dextro leucine]: PD, pharmacology
ethylketazocine: PD, pharmacology
naloxone: PD, pharmacology
metenkephalin[6 arginine 7 phenylalanine]: PD, pharmacology
proenkephalin: PD, pharmacology
beta endorphin: PD, pharmacology
alpha neoendorphin: PD, pharmacology
dynorphin B: PD, pharmacology
kappa opiate receptor: EC, endogenous compound
mu opiate receptor: EC, endogenous compound
delta opiate receptor: EC, endogenous compound
levacetylmethadol: PD, pharmacology
somatostatin: PD, pharmacology
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: CM, drug comparison
enkephalin[2 dextro alanine 4 methylphenylalanine 5 glycine]: PD, pharmacology
enkephalin[2,5 dextro penicillamine]: CM, drug comparison
enkephalin[2,5 dextro penicillamine]: PD, pharmacology
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide: CM, drug comparison
n methyl n [7 (1 pyrrolidinyl) 1 oxaspiro[4.5]dec 8 yl]benzeneacetamide: PD, pharmacology